5XCC0 Biopotential and Neural Interface Circuits

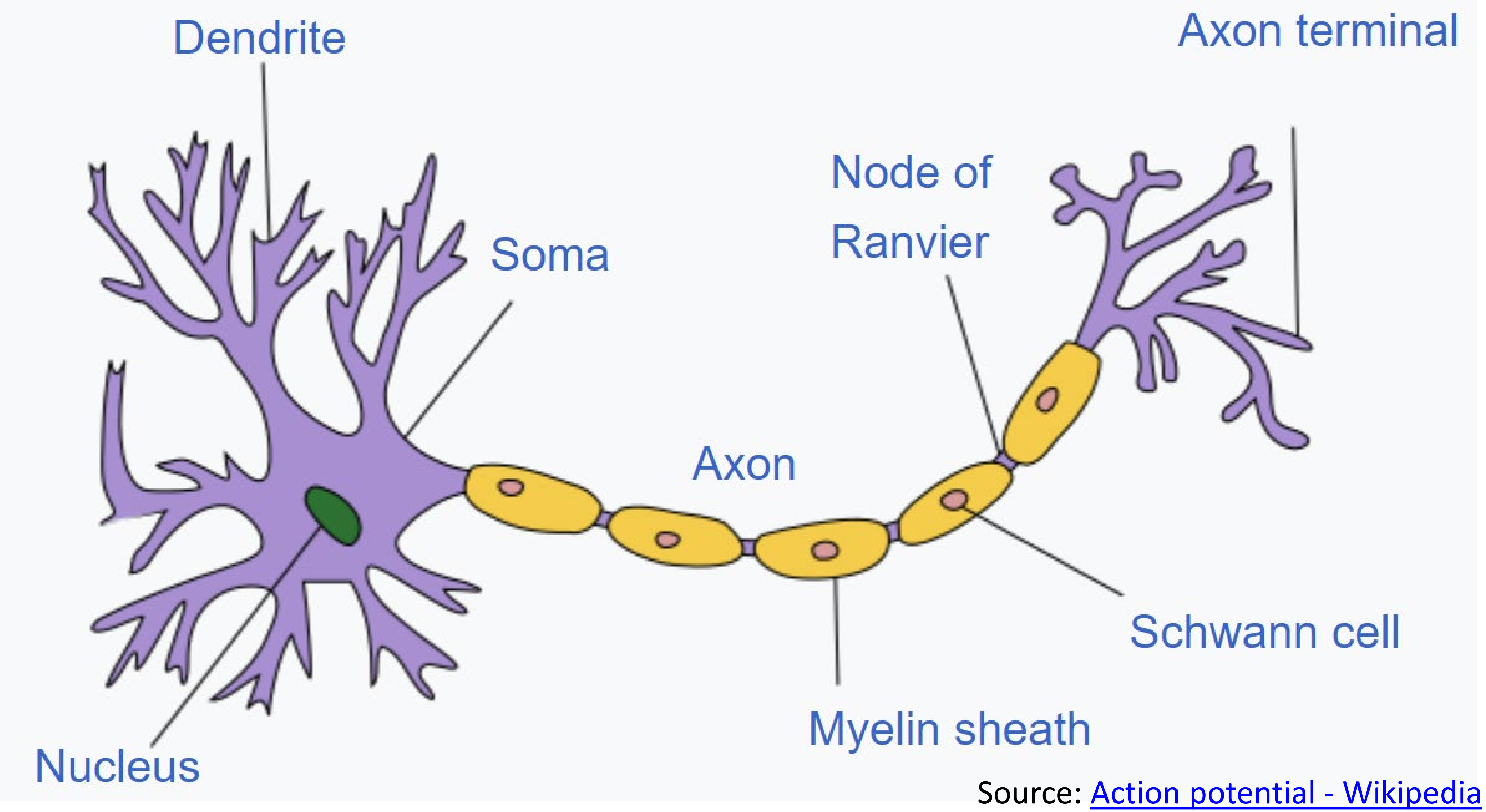
Acquisition of neural signals

Eugenio Cantatore

Outline

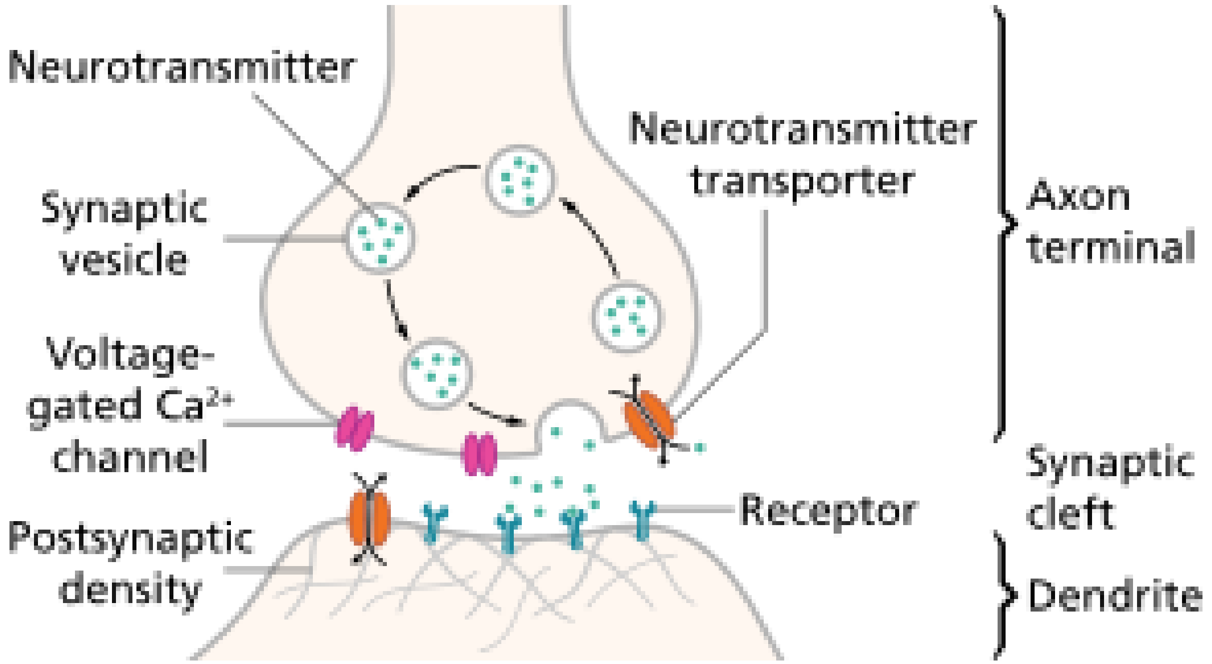
- Basic neurophysiology
- Example of a Neural Field Potential acquisition system
- Examples of Action Potentials acquisition systems

Neuron structure



Source: [Action potential - Wikipedia]

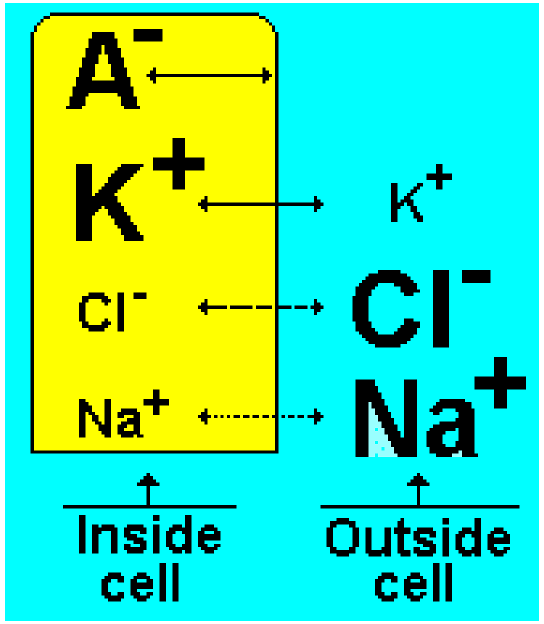
Synapses

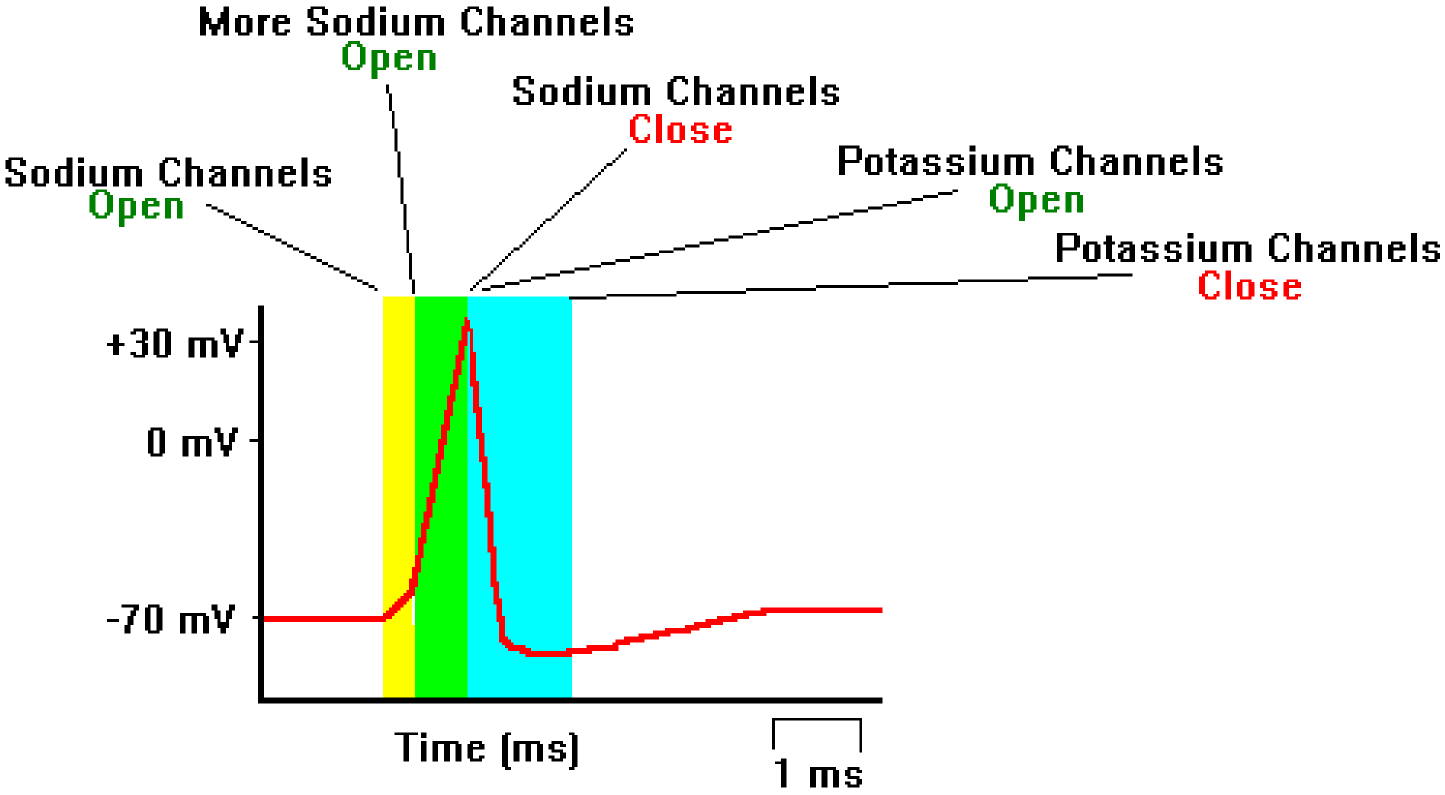


Source: [Action potential - Wikipedia]

Action potential

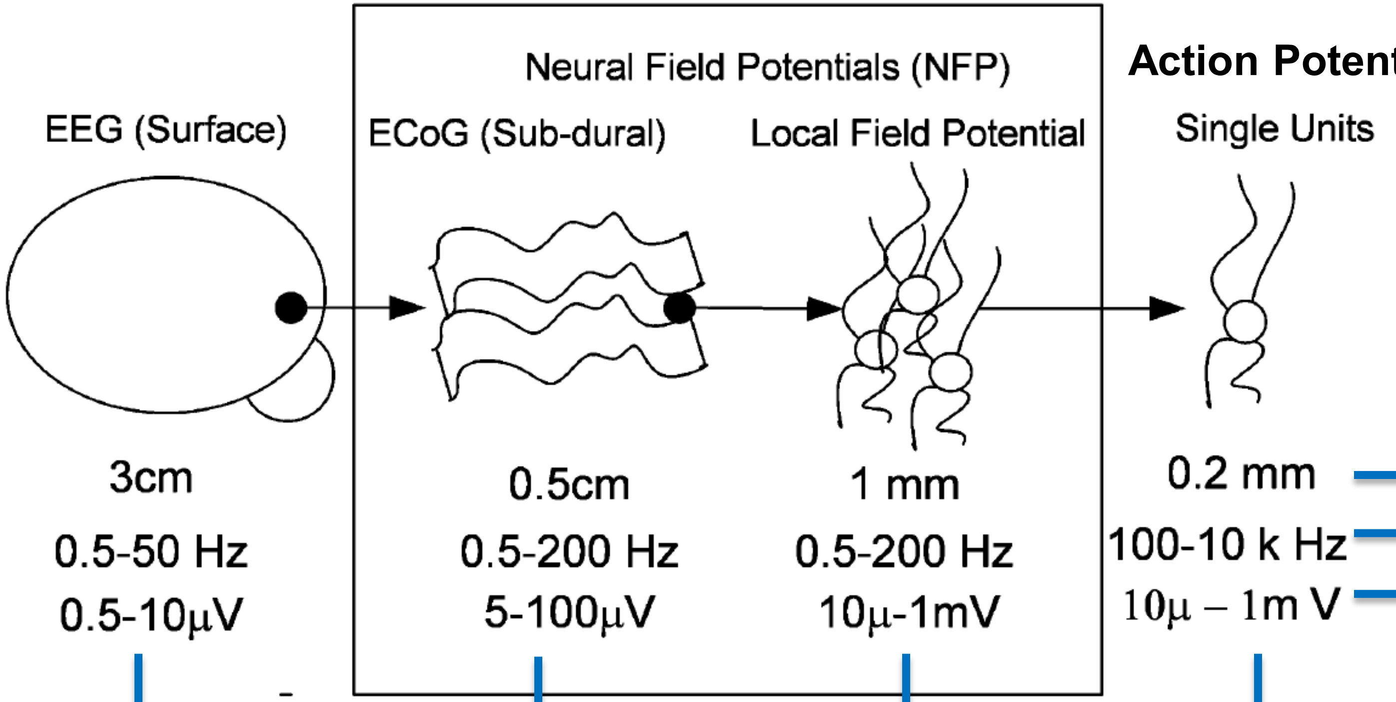
Charges at rest state

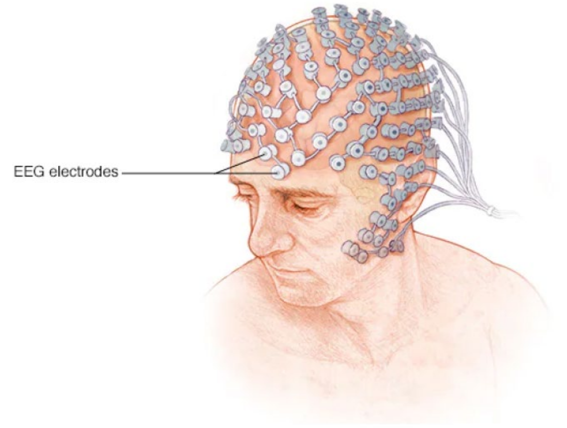




Source: [Neuroscience For Kids - action potential]

Neural signals with application examples





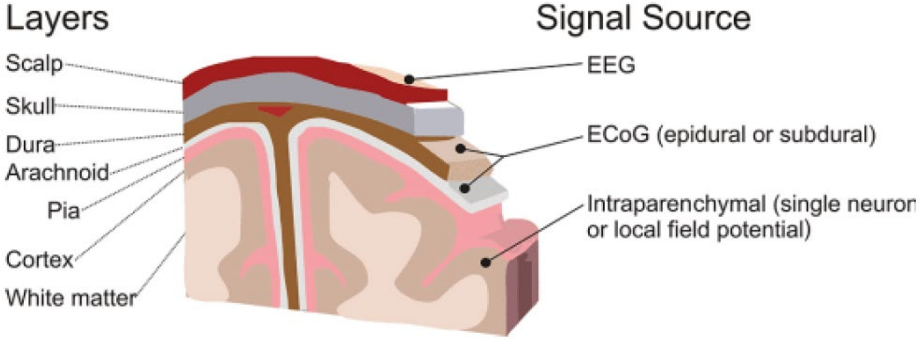
Spatial Resolution
Bandwidth
Amplitude

Monitor, predict and control epilectic seizures

Brain-machine interfaces, prosthetic control

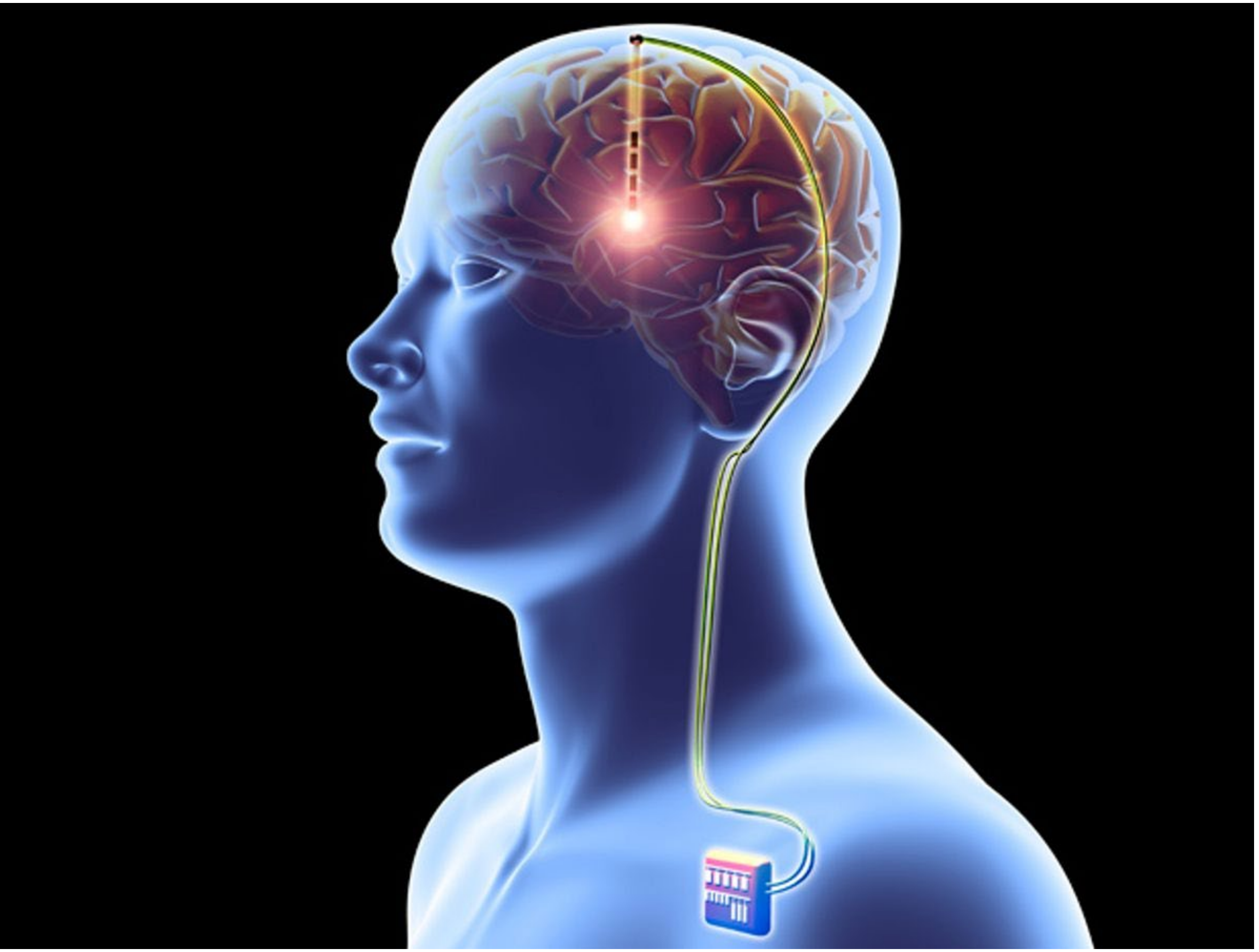
Closed loop neuro modulation

Neuroscience investigations



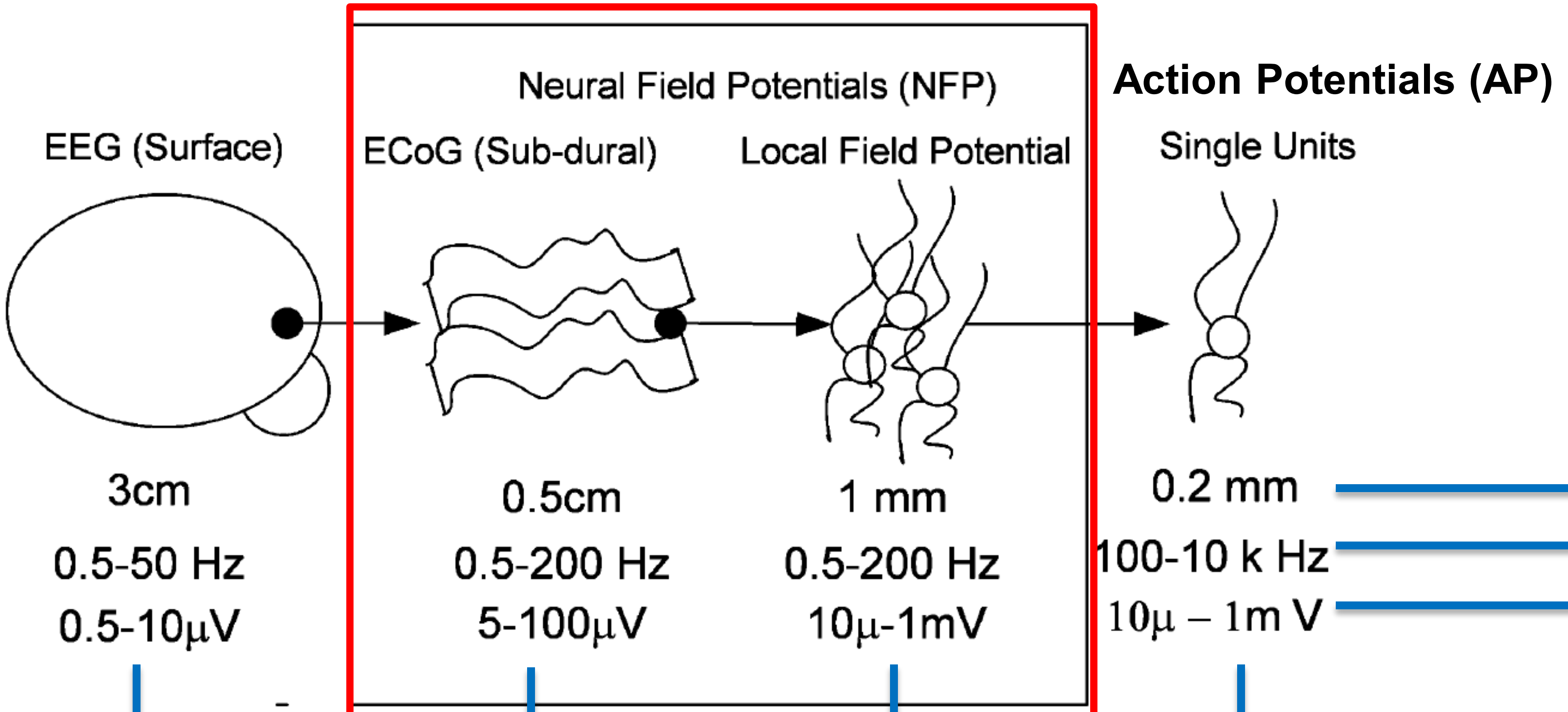
Source: T. Denison et al, JSSC 2007

Deep Brain Stimulation



- Parkinson's disease
- Essential tremor
- Dystonia
- Epilepsy
- Obsessive-compulsive disorder
- Amazing DBS Before & After | 225-769-2200 | Baton Rouge Parkinson's Specialists - YouTube

Neural signals with application examples



Spatial Resolution
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Source: T. Denison et al, JSSC 2007

Example of a NFP acquisition system

2934 IEEE JOURNAL OF SOLID-STATE CIRCUITS, VOL. 42, NO. 12, DECEMBER 2007

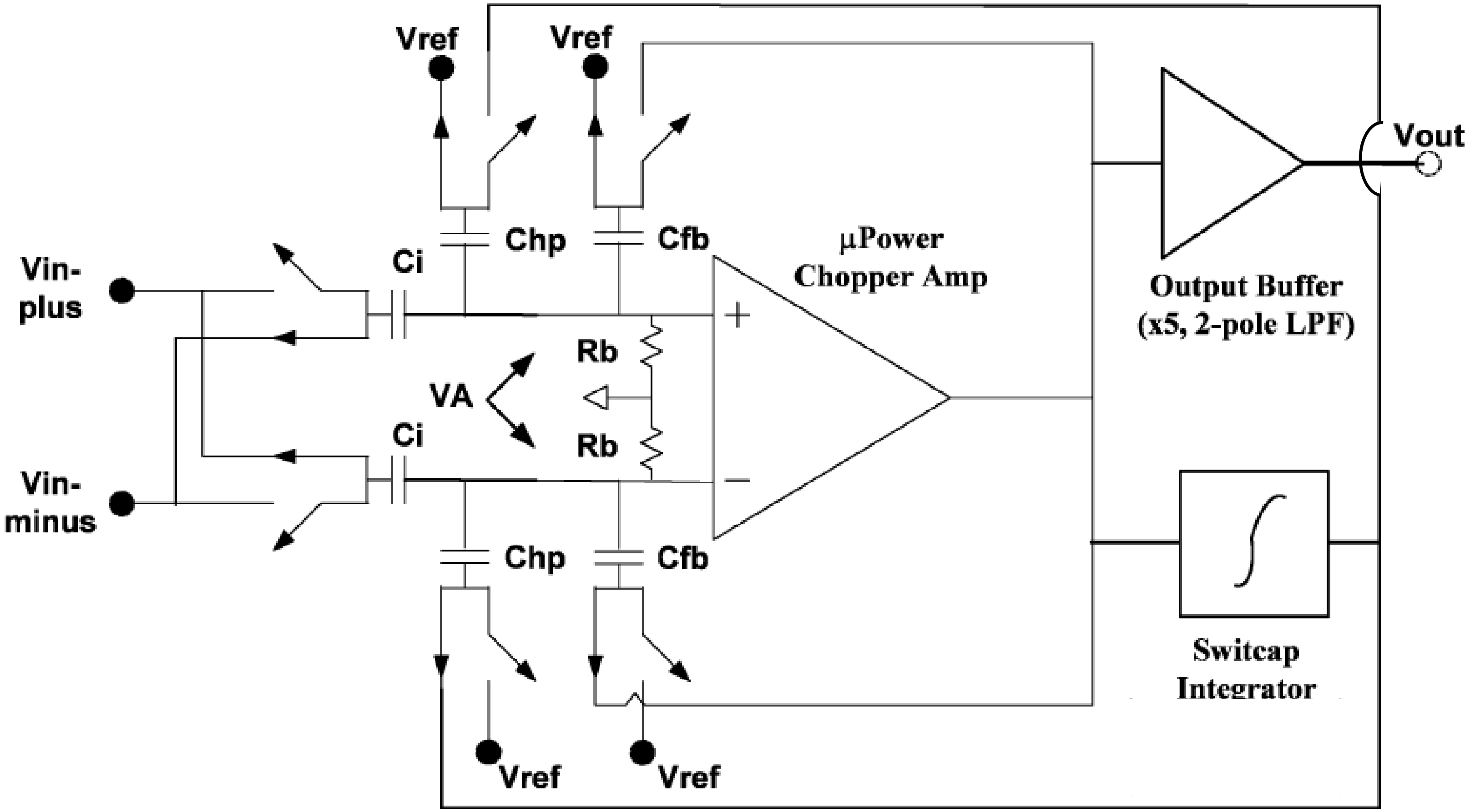
A 2 μW 100 nV/rtHz Chopper-Stabilized Instrumentation Amplifier for Chronic Measurement of Neural Field Potentials

Tim Denison, Kelly Consoer, Wesley Santa, Al-Thaddeus Avestruz, John Cooley, and Andy Kelly, *Member, IEEE*

- Medtronic work, meant for future applications:
  - Neuro prosthesis
  - Closed-loop neuromodulation (Epilepsy, Parkinson’s)

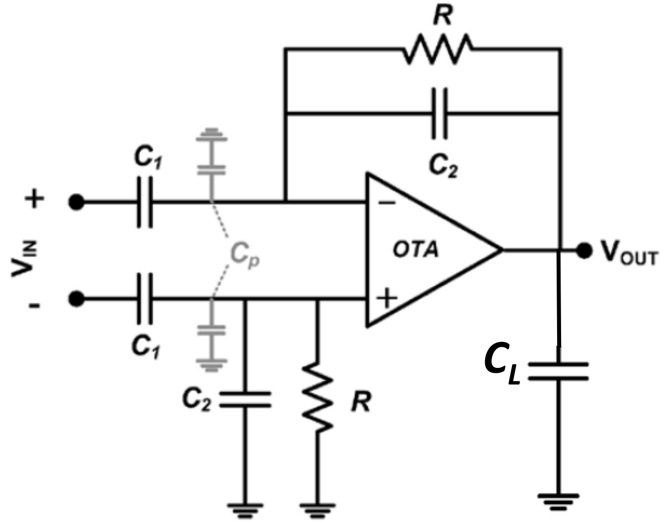
Example of a NFP acquisition system

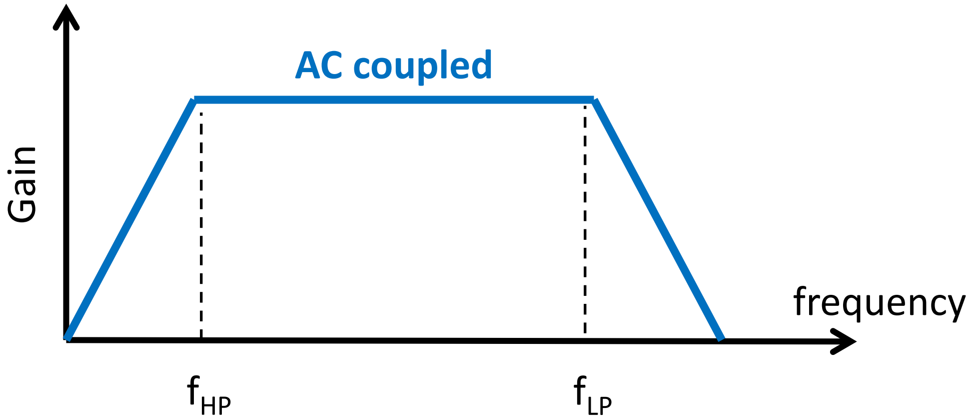
- Based on a capacitive-feedback amplifier



Example of a NFP acquisition system

- Main properties of capacitive-feedback amplifier





$$A_0 = \frac{C_1}{C_2} \quad \text{(in band)}$$

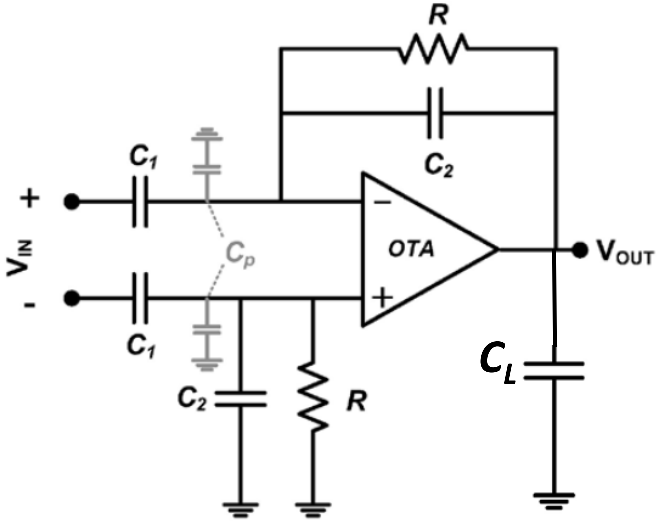
$$f_{HP} = \frac{1}{2\pi R C_2}$$

$$f_{LP} \approx \frac{g_m}{2\pi A_0 C_L}$$

$$v_{IRN}^2 = \left(\frac{C_1 + C_2 + C_P}{C_1} \right)^2 v_{OTA}^2$$

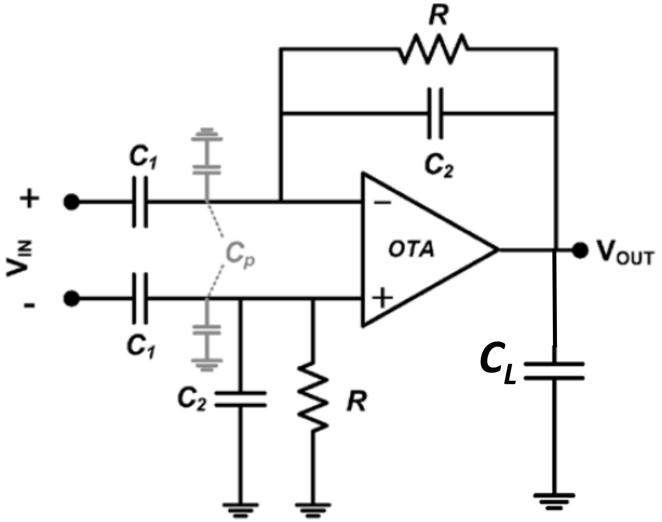
$$Z_{in} \approx \frac{1}{j\omega C_1}$$

Example of a NFP acquisition system



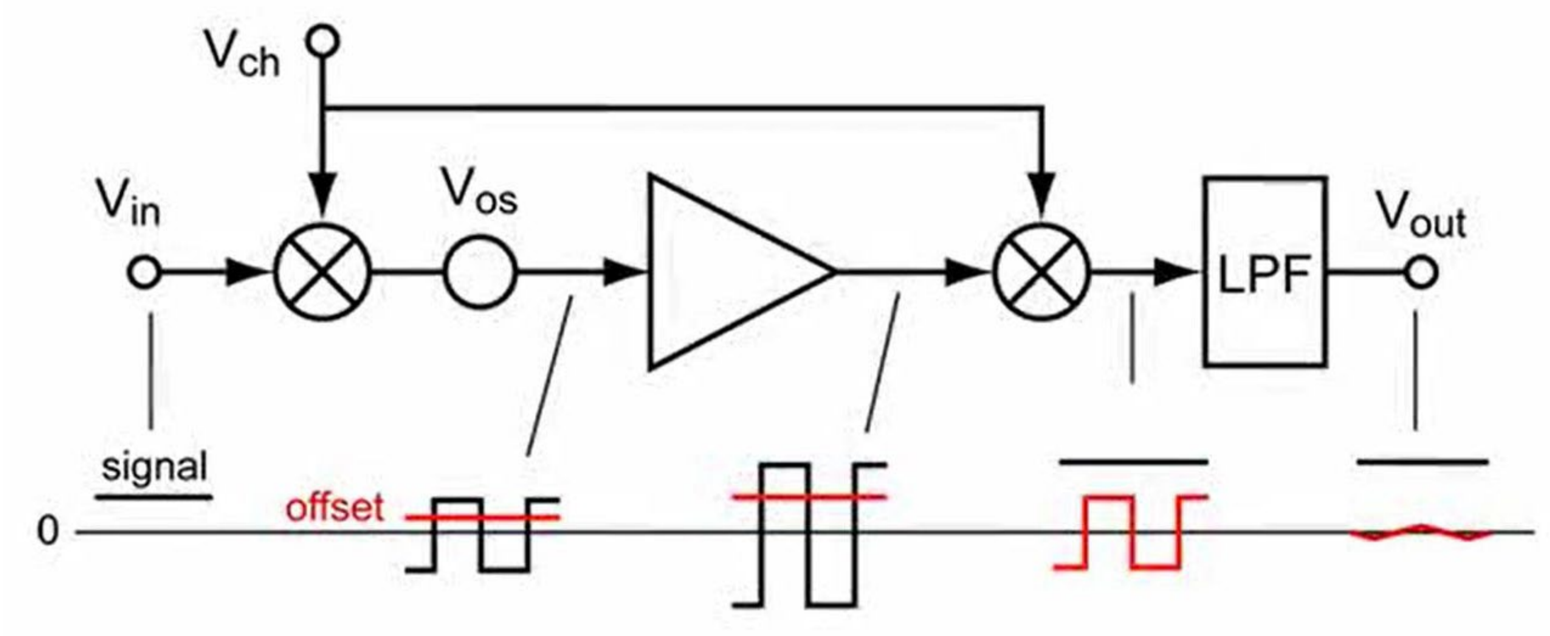
- Important trade-offs:
  - To improve 1/f noise, increase area of OTA input transistors
  - This increases C_p and thus worsens V_{IRN}

Example of a NFP acquisition system



- Important trade-offs:
  - To improve 1/f noise, apply chopping
  - Chopping increases the frequency of the signal applied to C_1 and thus results in larger input current and lower input impedance

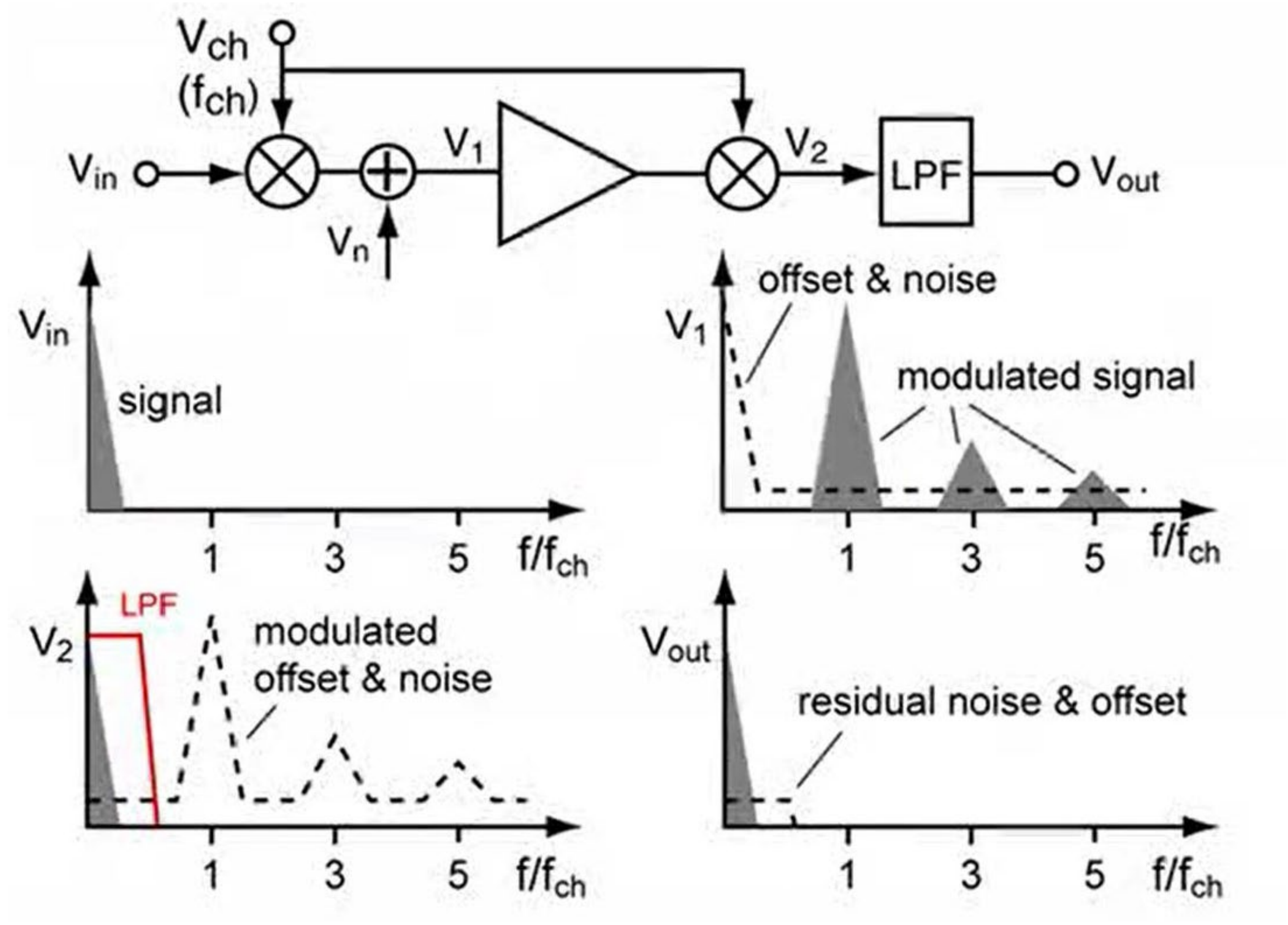
Intermezzo: chopping in time domain



- Chopping duty cycle must be exactly 50% to avoid a DC component in the modulated offset at the output.

Source: [K. Makinwa, Dynamic-Offset Cancellation Techniques in CMOS]()

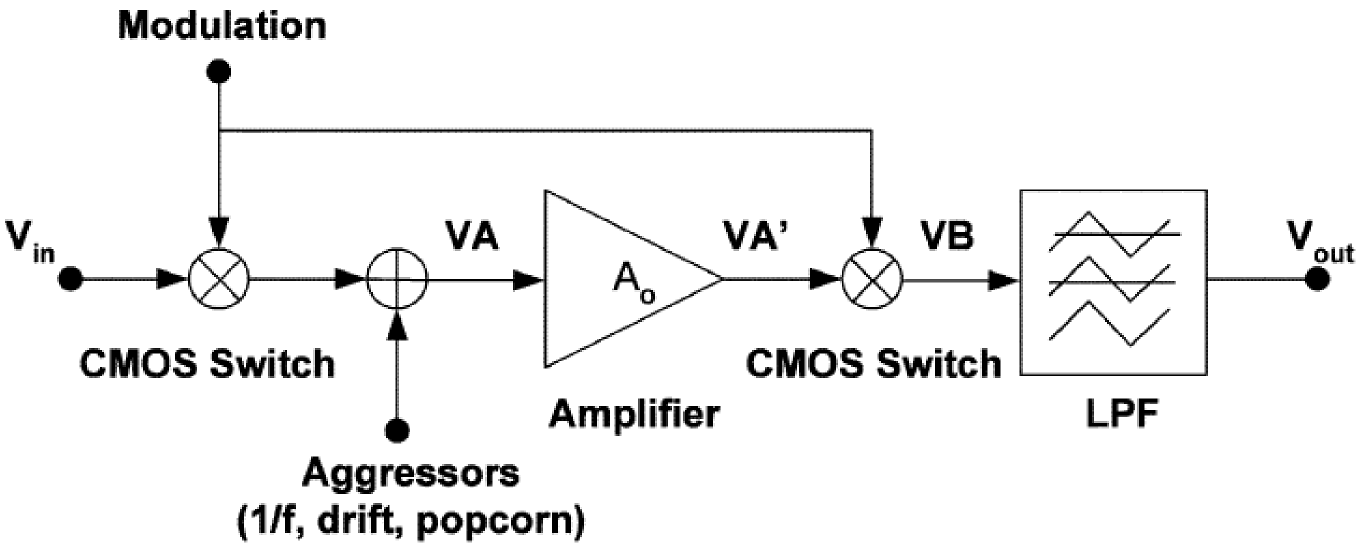
Intermezzo: chopping in frequency domain



Source: [K. Makinwa, Dynamic-Offset Cancellation Techniques in CMOS]()

Example of a NFP acquisition system

- Drawbacks of chopping:
  - The amplifier must have large bandwidth to cope with the chopped signal
  - Due to incomplete settling the gain when chopping is applied is not A_0



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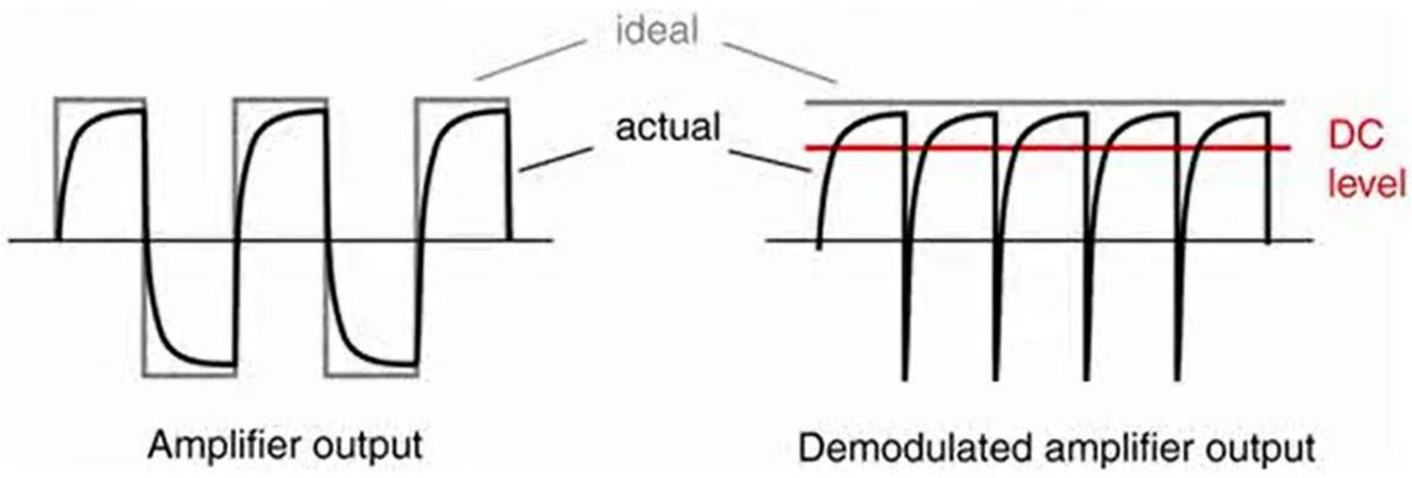
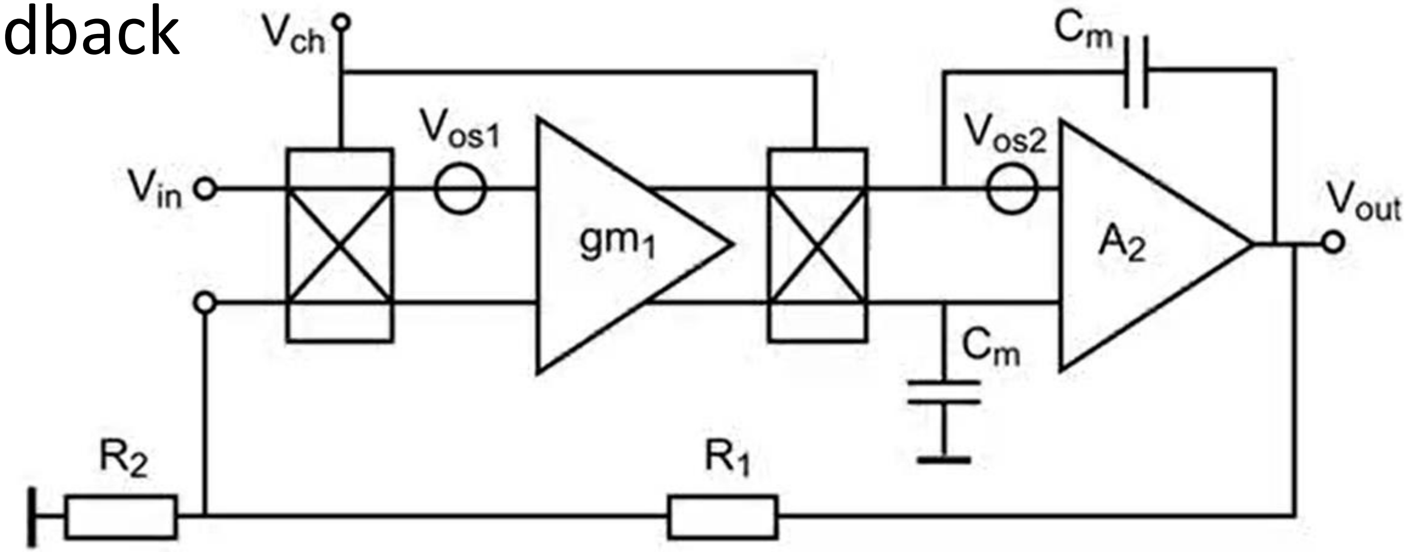


Source: [K. Makinwa, Dynamic-Offset Cancellation Techniques in CMOS]

Example of a NFP acquisition system

- To restore an accurate gain:
  - Apply feedback

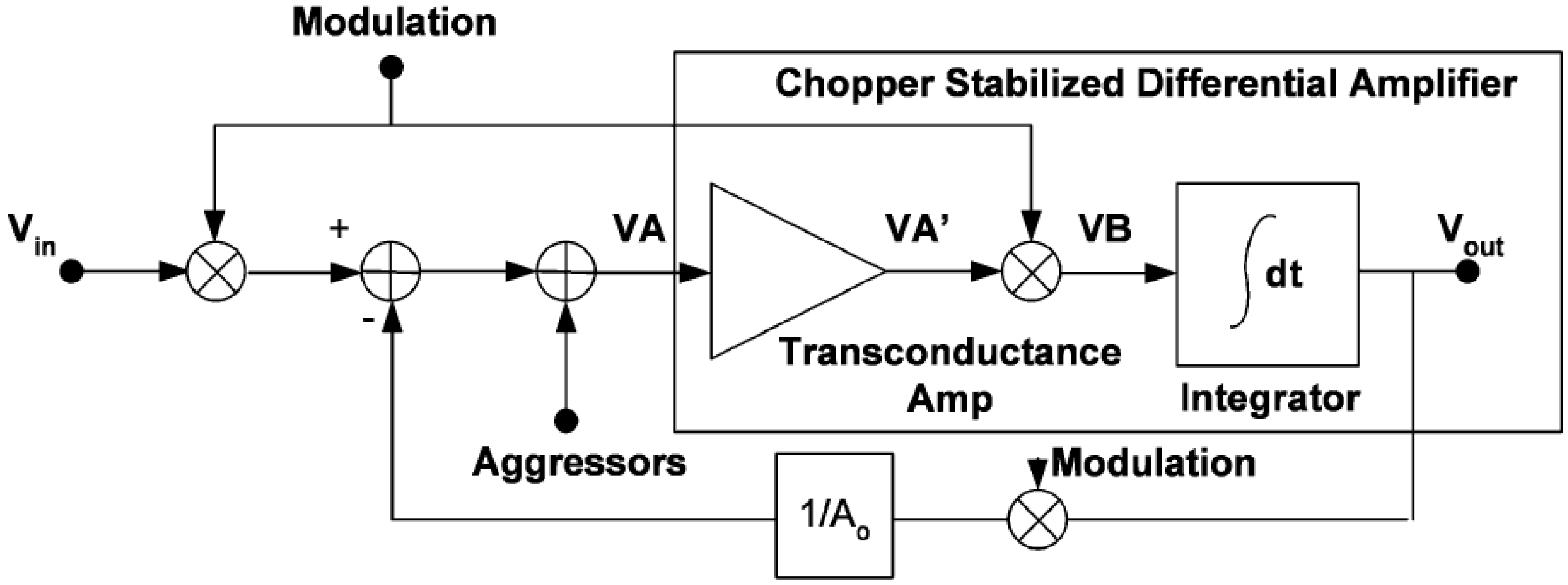


  - Resistor ratio accurately determines the gain
  - Miller capacitance help to suppress ripple
  - DC gain of first stage must be large enough to suppress V_{OS2} at input
  - Higher chopping frequency reduces ripple

Source: [K. Makinwa, Dynamic-Offset Cancellation Techniques in CMOS]

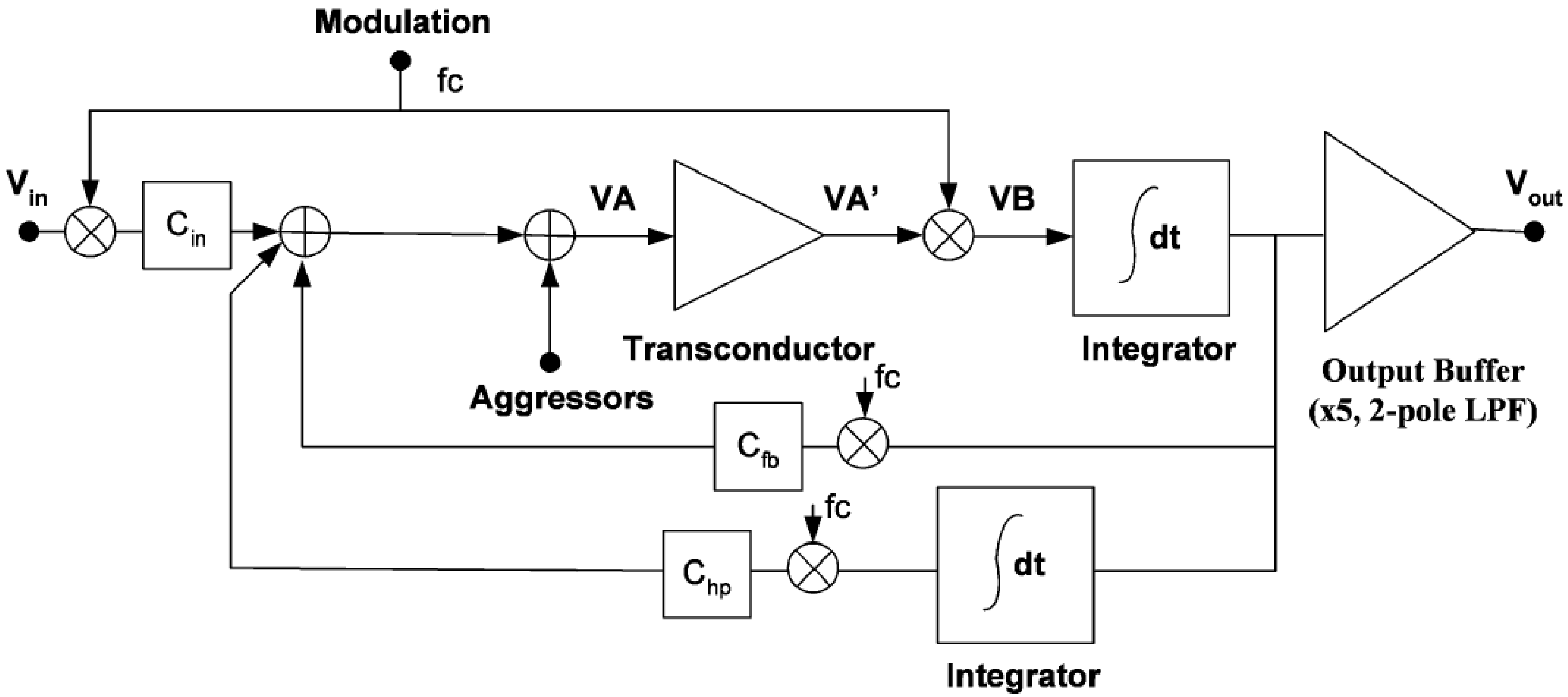
Example of a NFP acquisition system

- To restore an accurate gain:
  - Apply feedback



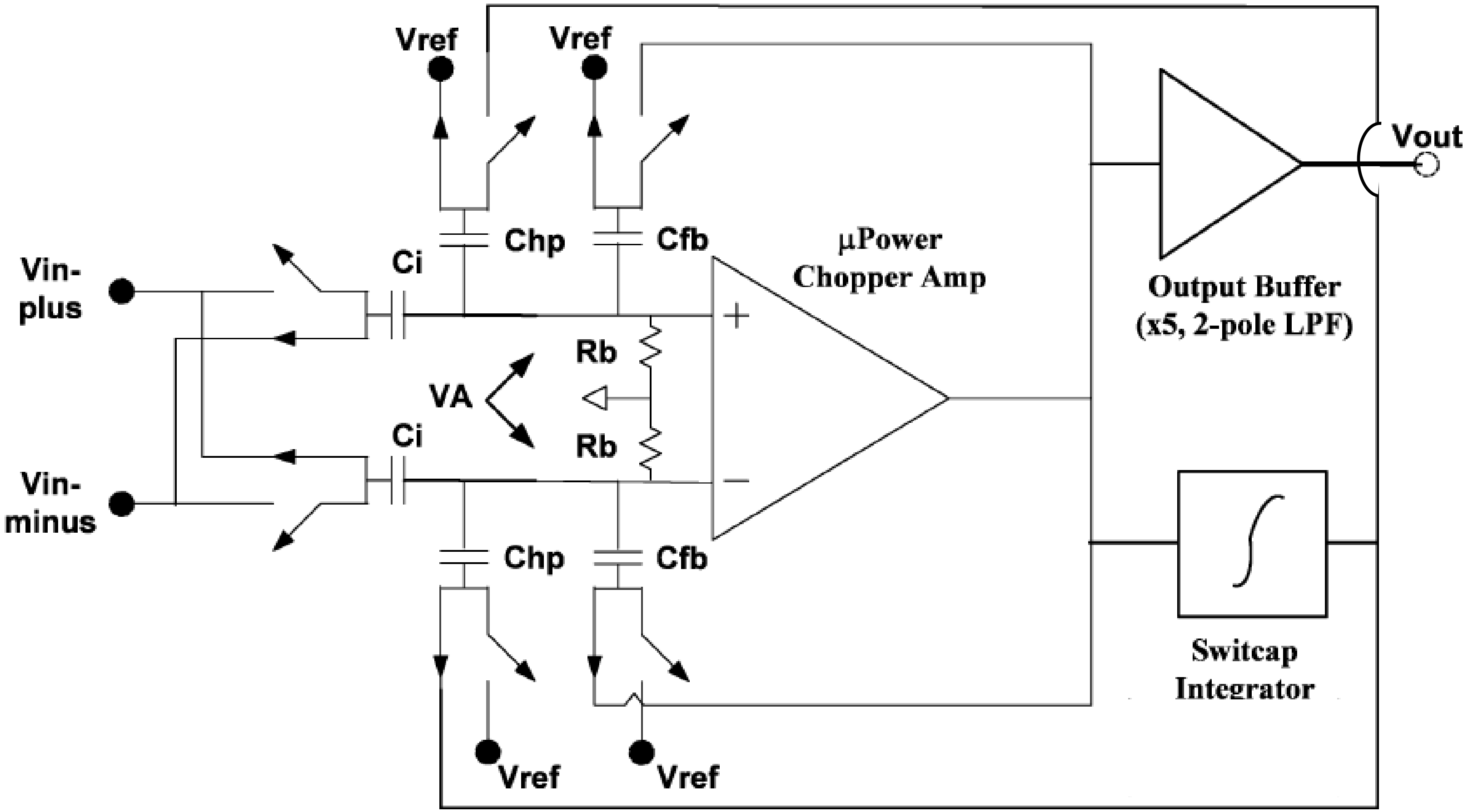
Example of a NFP acquisition system

- Using an integrator in the feedback
  - Feedback in the chopped domain enables use of capacitors as passives
  - A high-pass behavior can be obtained



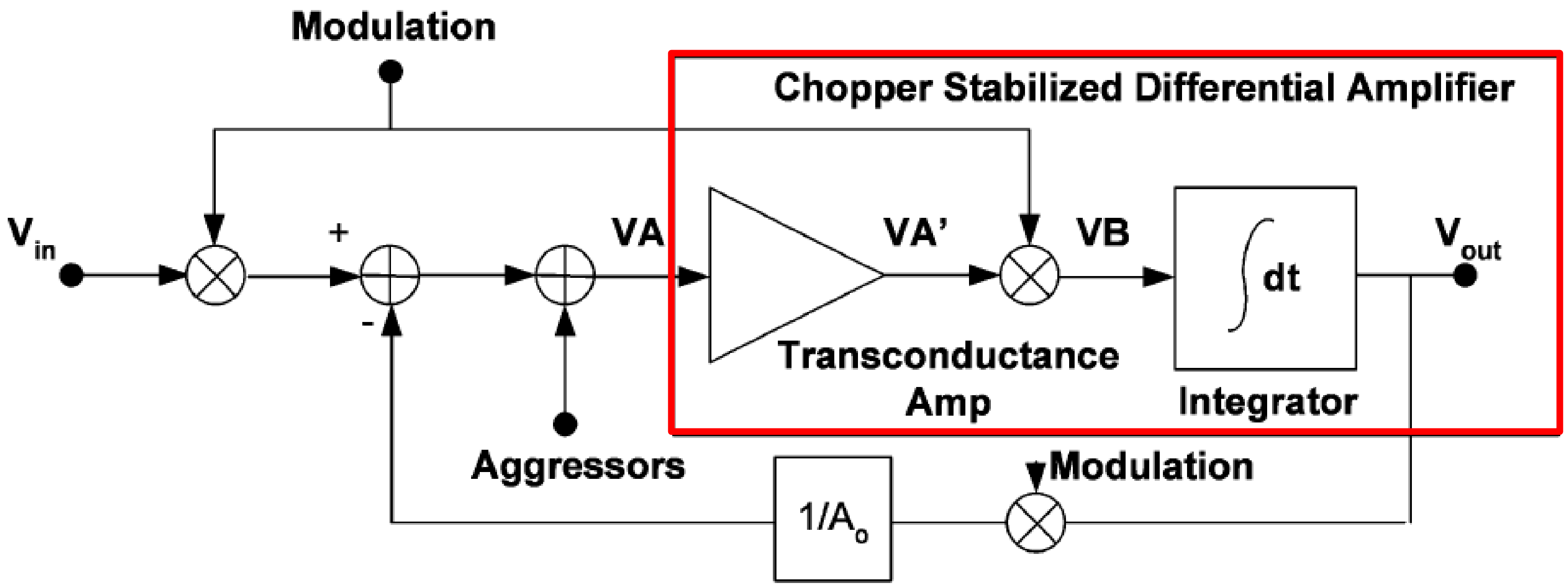
Example of a NFP acquisition system

- Resulting schematic



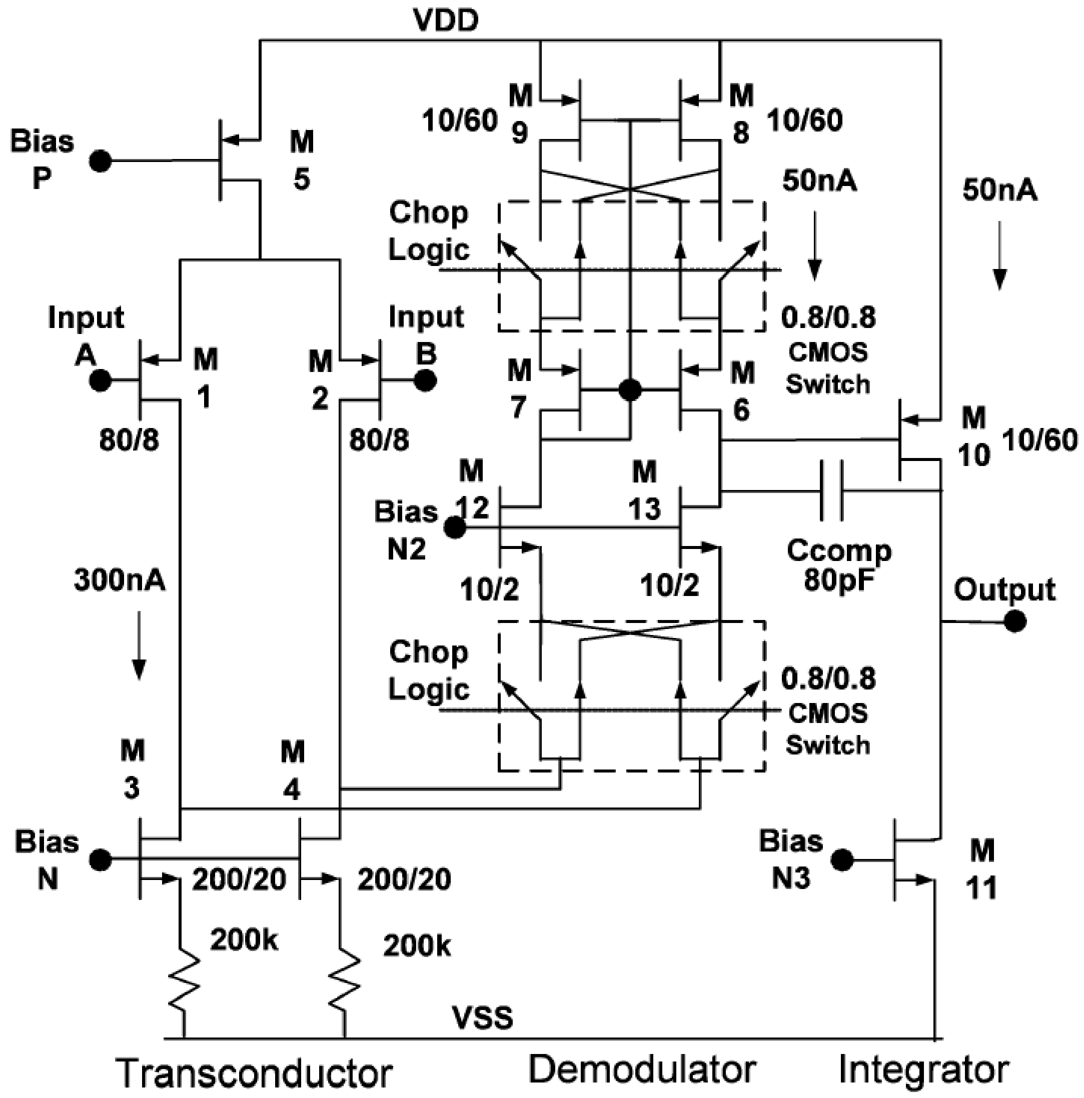
Example of a NFP acquisition system

- To restore an accurate gain:
  - Apply feedback
  - Feedback in the chopped domain enables use of capacitors as passives



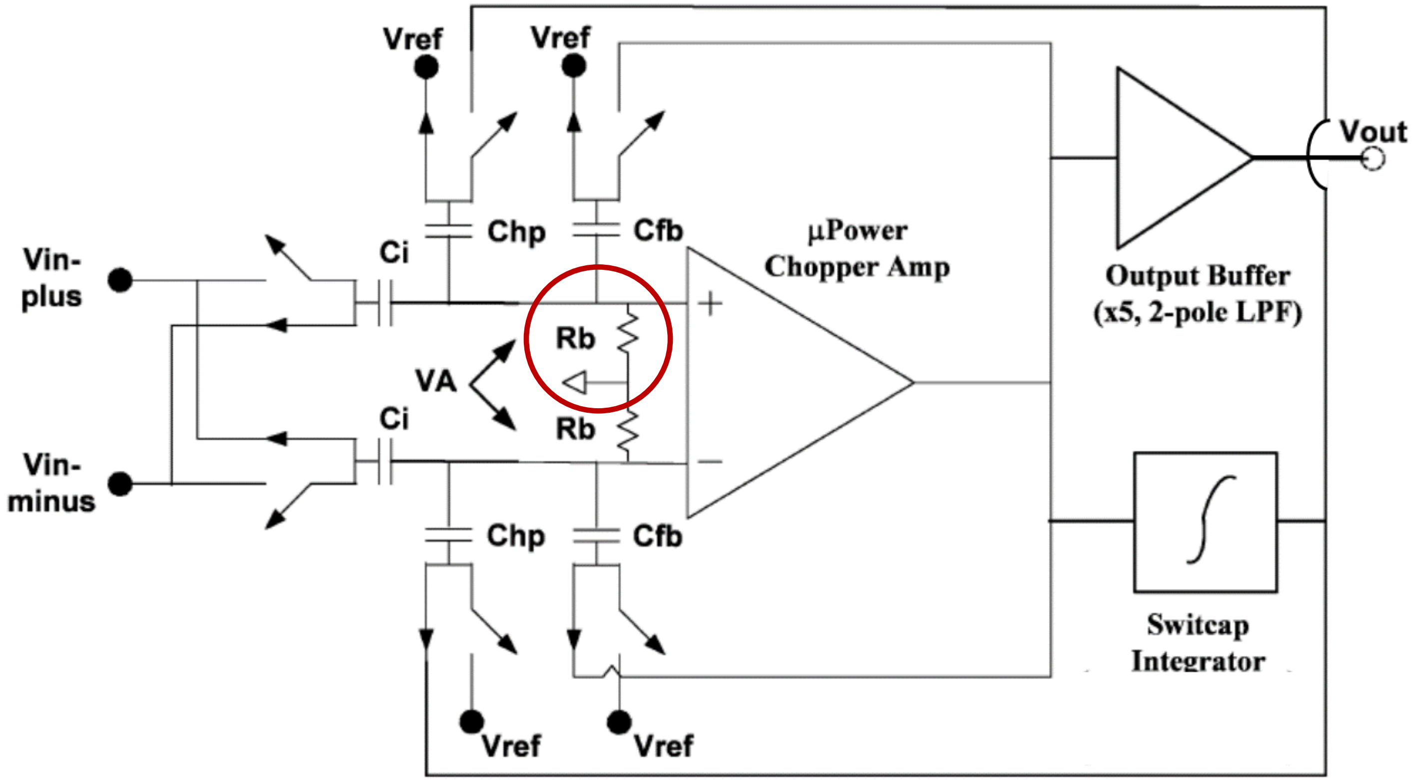
Example of a NFP acquisition system

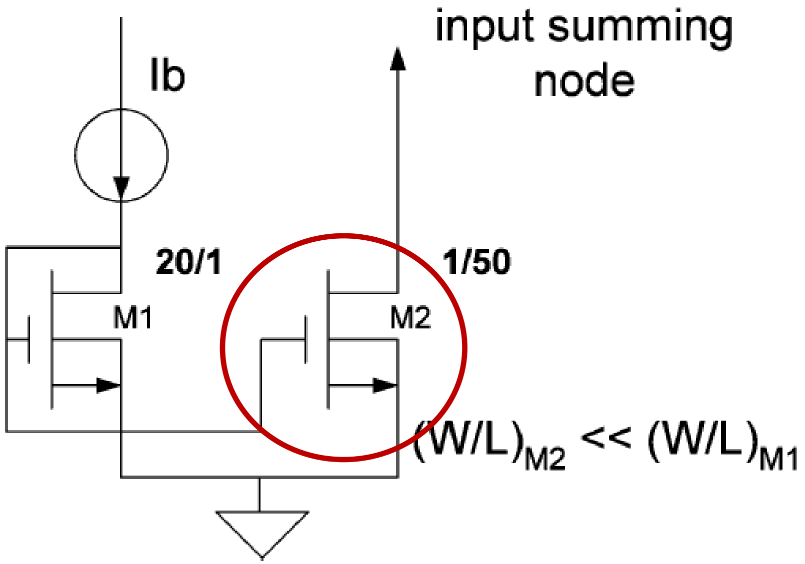
- Amplifier schematic



Example of a NFP acquisition system

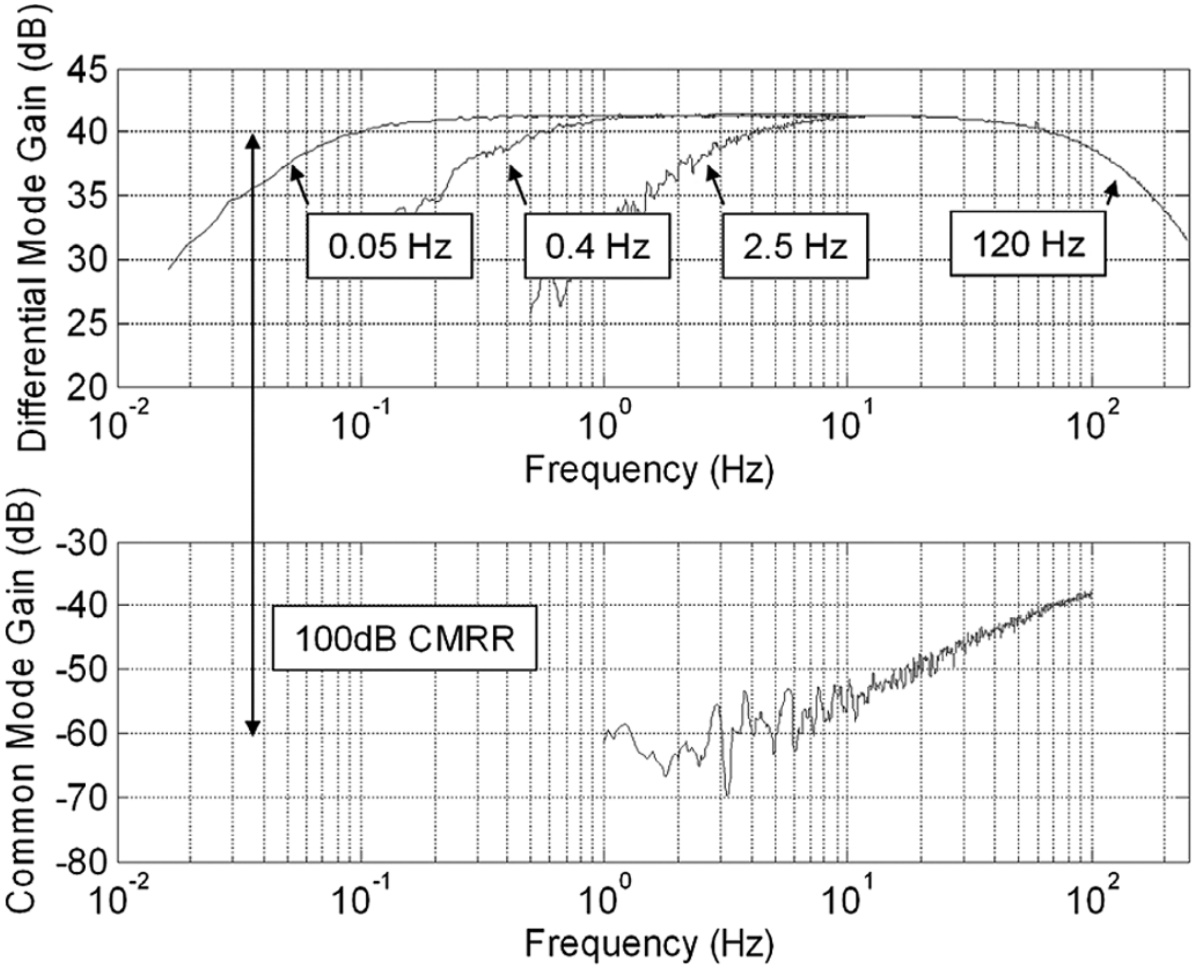
- Implementation of Rb

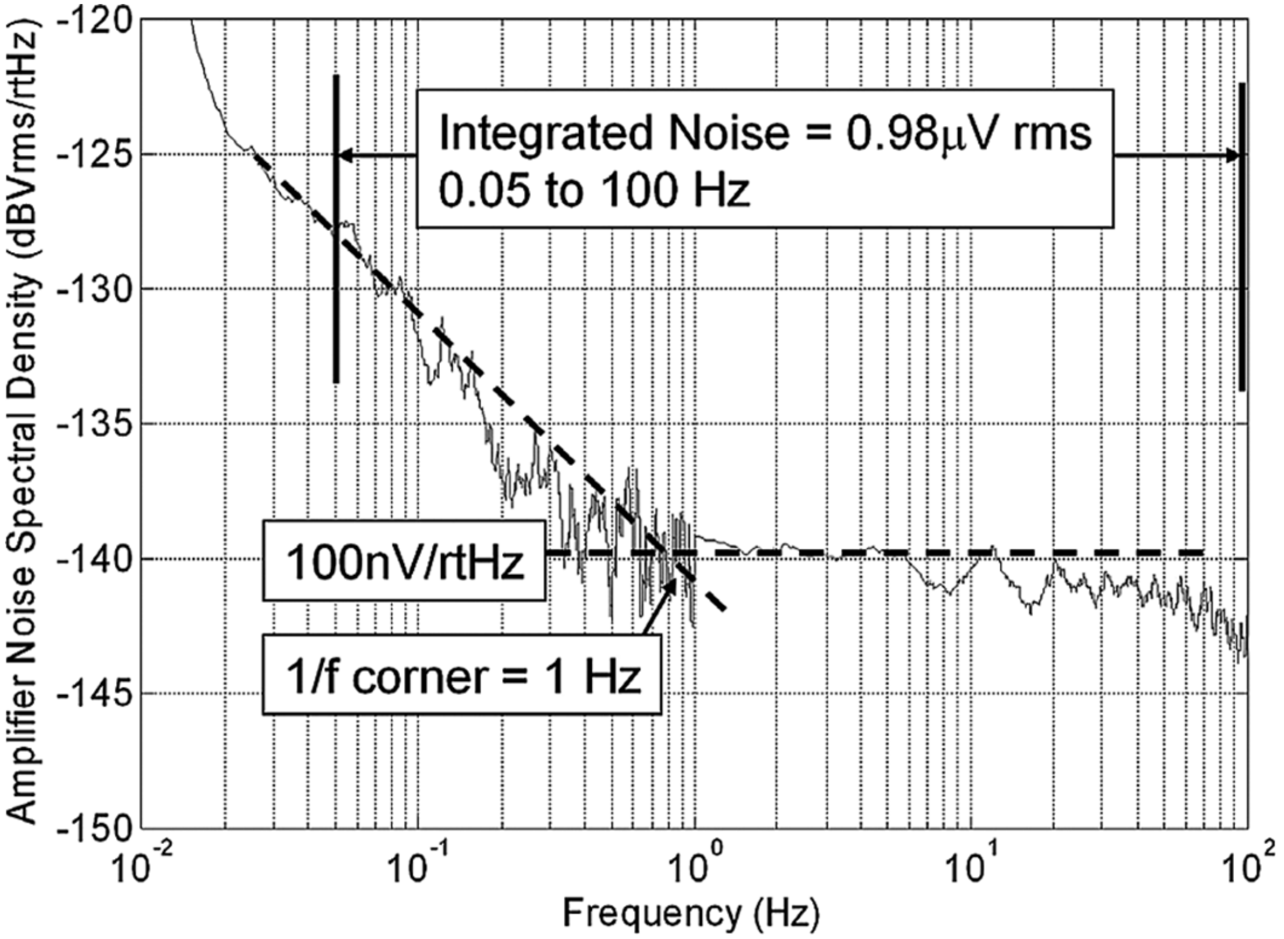




Example of a NFP acquisition system

- Implementation results





Example of a NFP acquisition system

- Specifications and their experimental validation

BIOPOTENTIAL AMPLIFIER SPECIFICATIONS

Specification	Value	Units/Comments
Supply Voltage	1.7 to 3.3	Volts
Supply Current	1.0	uA
Gain	40 (min)	dB
Noise	1.5	μV rms , 0.05 to 100Hz
CMRR	> 80	dB (DC to 60Hz)
Nonlinearity	< 0.1%	Harmonic Distortion
Aliasing	< -40	dB (compared to baseband)
Functional Range	20 to 45	Celsius
High-Pass Corners	0.05, 0.4, 2.5	Hz, no external components
Electrode Polarization	15, 50	mV (DC headroom)
Lowpass Corner Freq	150	Hz / corner frequency

KEY BIOPOTENTIAL AMPLIFIER RESULTS

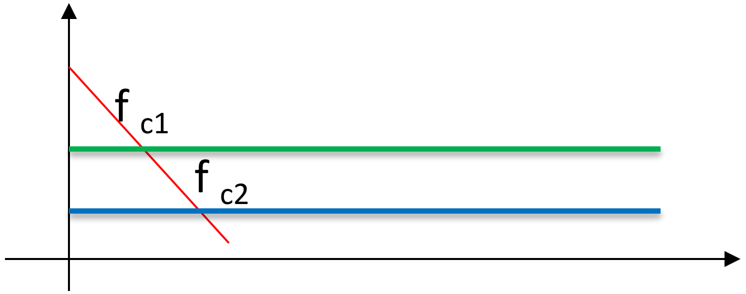
Specification	Value	Units/Comments
Supply Voltage	1.8 to 3.3	Volts
Supply Current	1.0	uA
Gain	41, 50.5	dB (High polarization), (Diagnostic)
Noise	0.95	μV rms , 0.05 to 100Hz
CMRR	> 80 > 100	SE dB (DC to 60Hz) DE dB (DC to 100Hz)
Nonlinearity	< 0.1%	Harmonic Distortion (5 mV input)
Aliasing	< -50	dB (compared to baseband)
NEF	4.6 / 5.4	Diagnostic / Sense-Stim Modes
High-Pass Corners	0.05, 0.4, 2.5	Hz, digitally programmable No external components
Lowpass Corner	180	Hz (-6dB, 2-pole filter)

Exercise 1

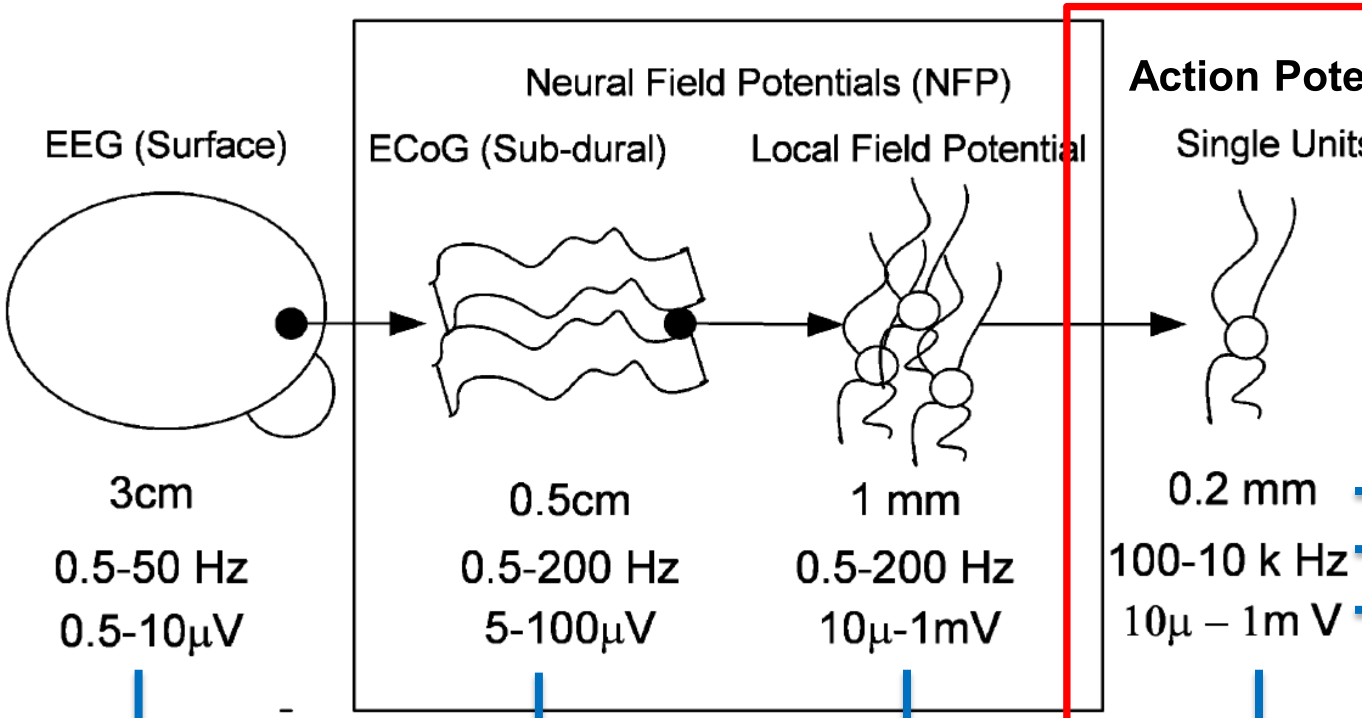
- Discuss whether this statement is correct or not and explain your answer:
  - In a biopotential interface circuit using chopping, the chopping frequency must be larger if the required total input integrated noise level is reduced

Exercise 1: answer

- The statement is correct:
  - In a circuit using chopping the residual noise after applying chopping is due to white noise (slide 15)
  - To reduce the input integrated noise, thus, one must lower the white noise level (for instance, from green to blue here below), e.g. increasing the current in the input transistors
  - This approach decreases the thermal noise but has little effect on the 1/f noise. Therefore, the noise corner is pushed to higher frequencies ($f_{c1} \rightarrow f_{c2}$). To be effective, chopping must be performed at frequencies higher than the noise corner, thus the chopping frequency must increase.



Neural signals with application examples



Spatial Resolution
Bandwidth
Amplitude

Monitor, predict and control epilectic seizures

Brain-machine interfaces, prosthetic control

Closed loop neuro modulation

Neuroscience investigations

Source: T. Denison et al, JSSC 2007

Example of an AP acquisition system

IEEE JOURNAL OF SOLID-STATE CIRCUITS, VOL. 42, NO. 1, JANUARY 2007 123

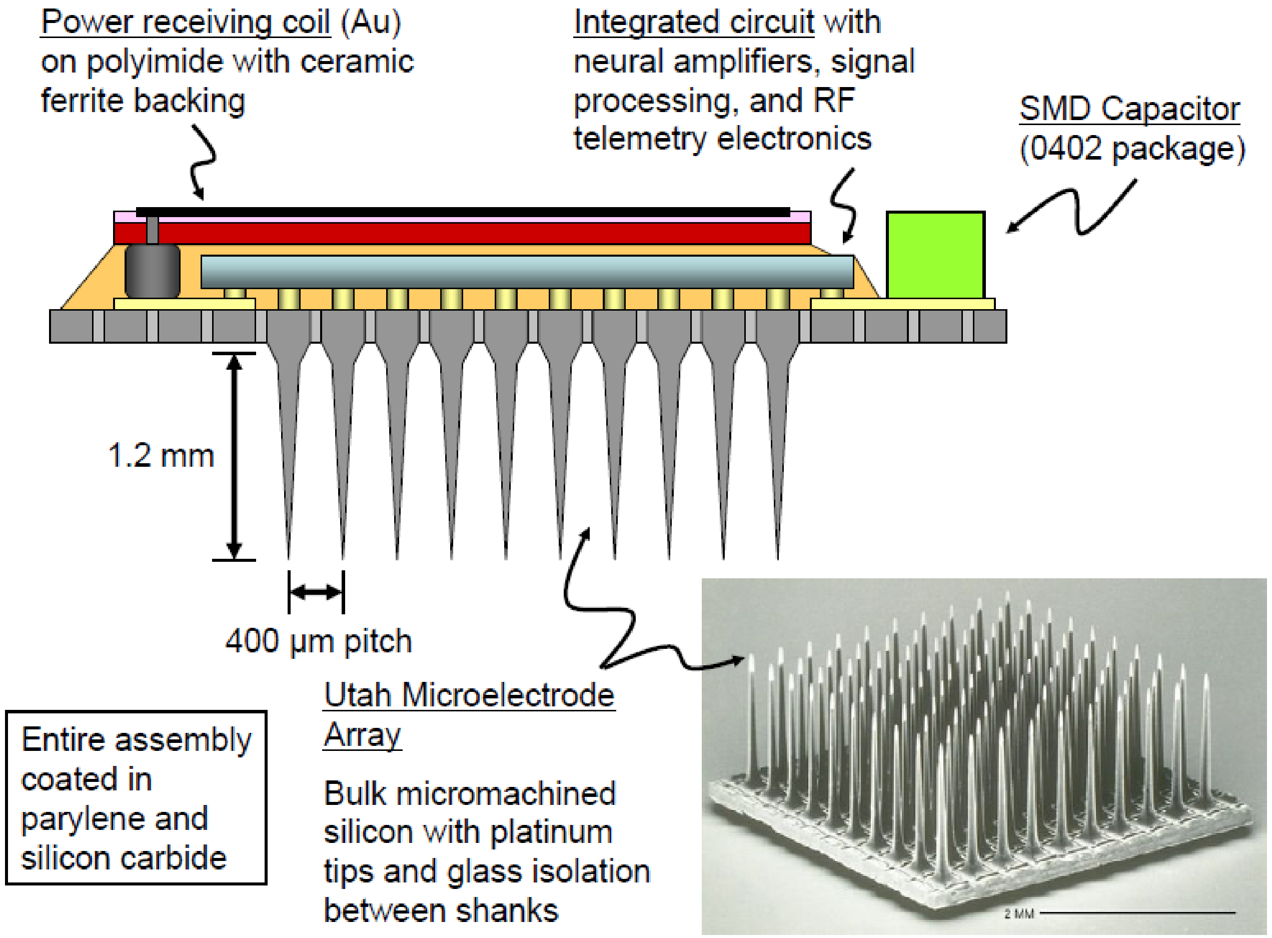
A Low-Power Integrated Circuit for a Wireless 100-Electrode Neural Recording System

Reid R. Harrison, *Member, IEEE*, Paul T. Watkins, *Student Member, IEEE*, Ryan J. Kier, *Student Member, IEEE*, Robert O. Lovejoy, Daniel J. Black, *Student Member, IEEE*, Bradley Greger, *Member, IEEE*, and Florian Solzbacher, *Member, IEEE*

- University of Utah work, related to Utah array development

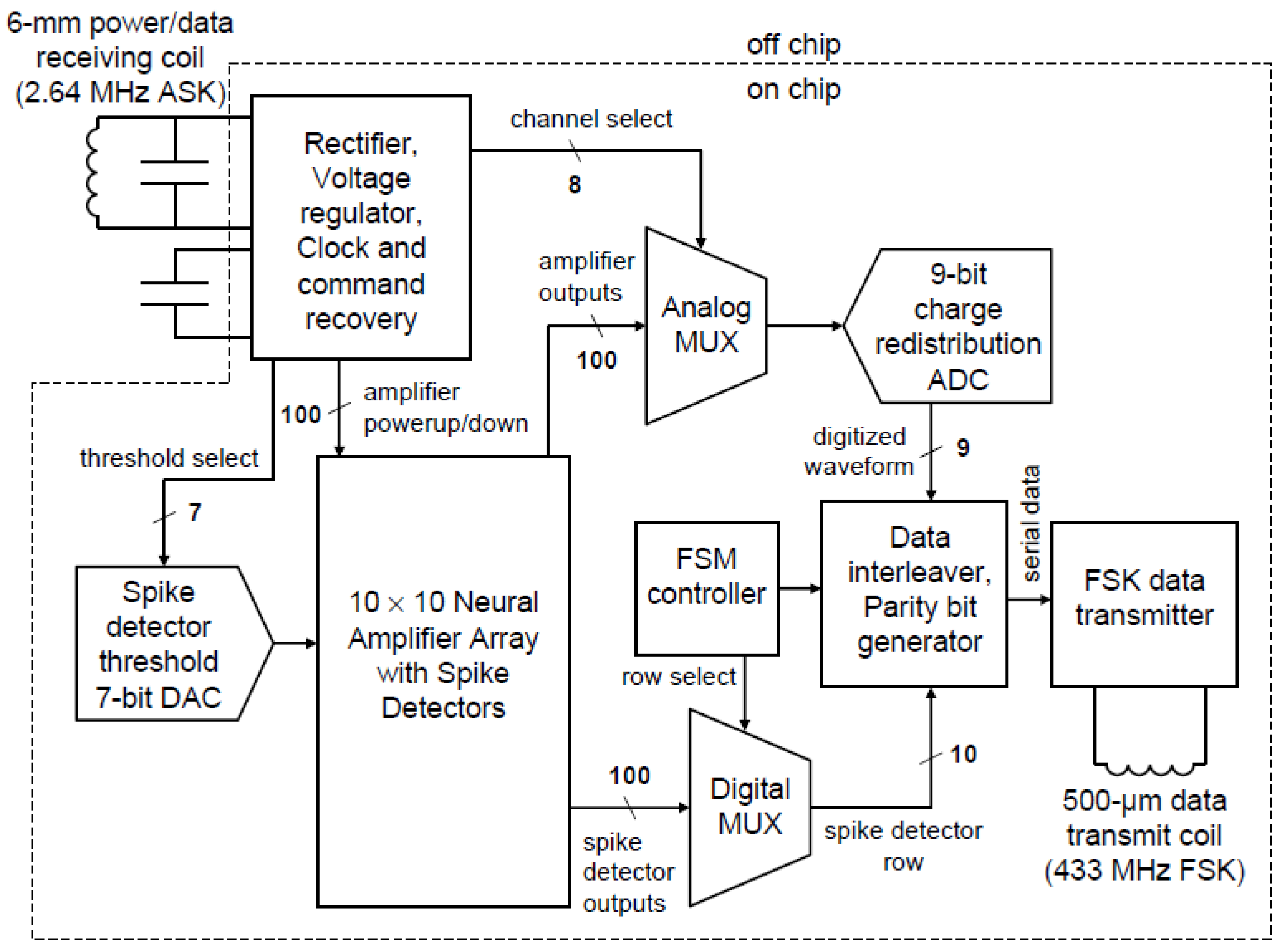
Example of an AP acquisition system

- System overview



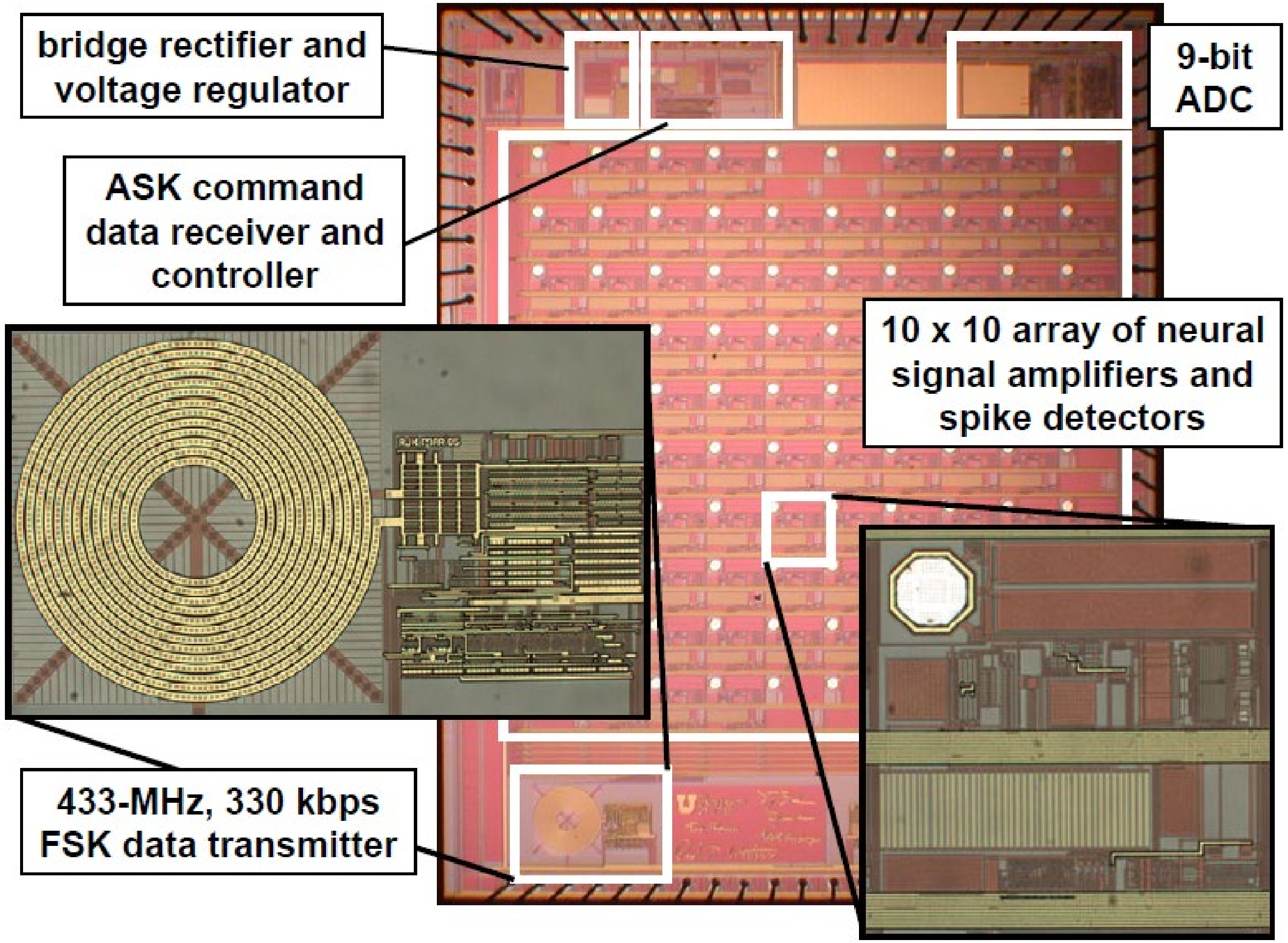
Example of an AP acquisition system

- Block diagram



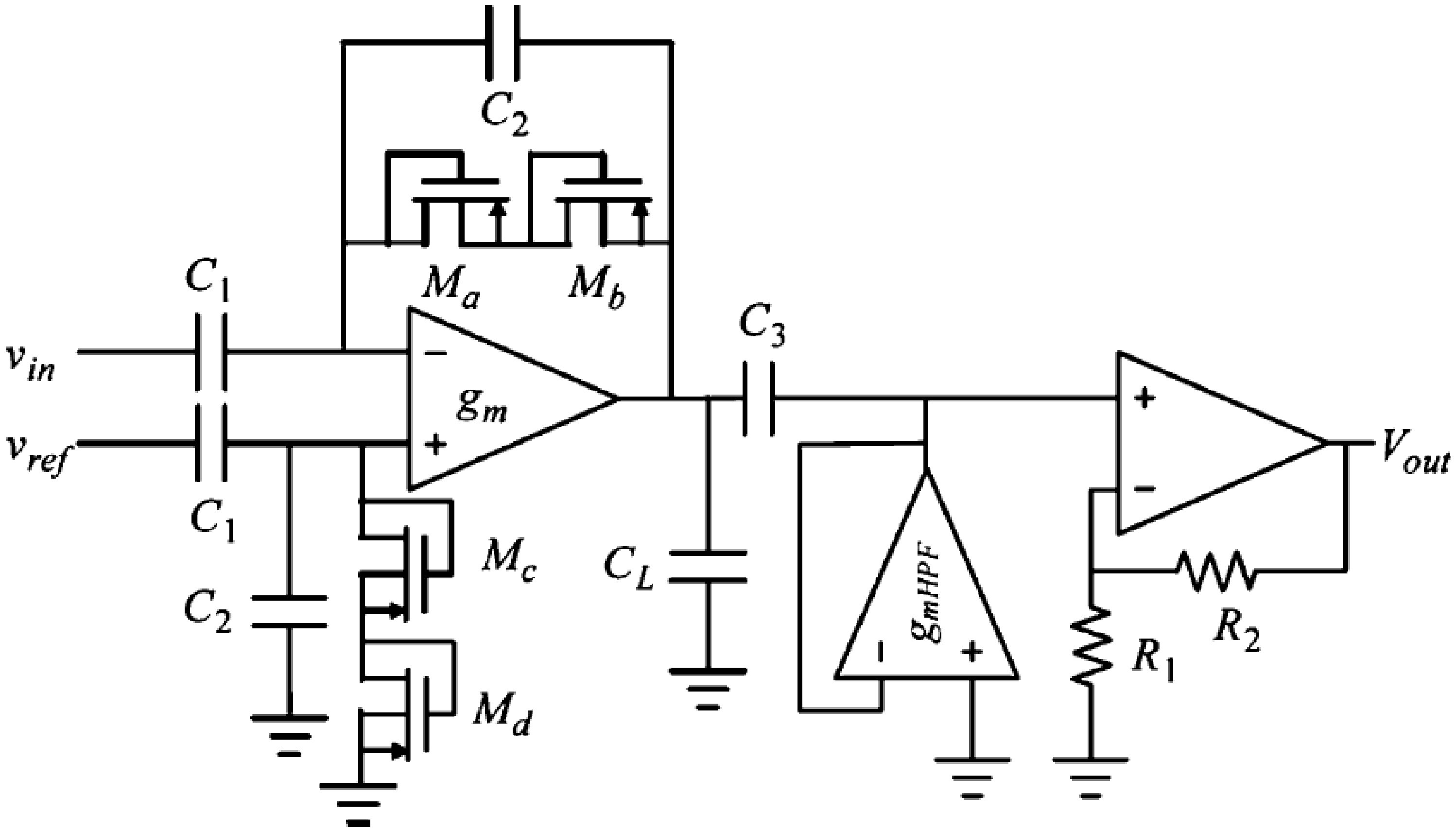
Example of an AP acquisition system

- Chip photos



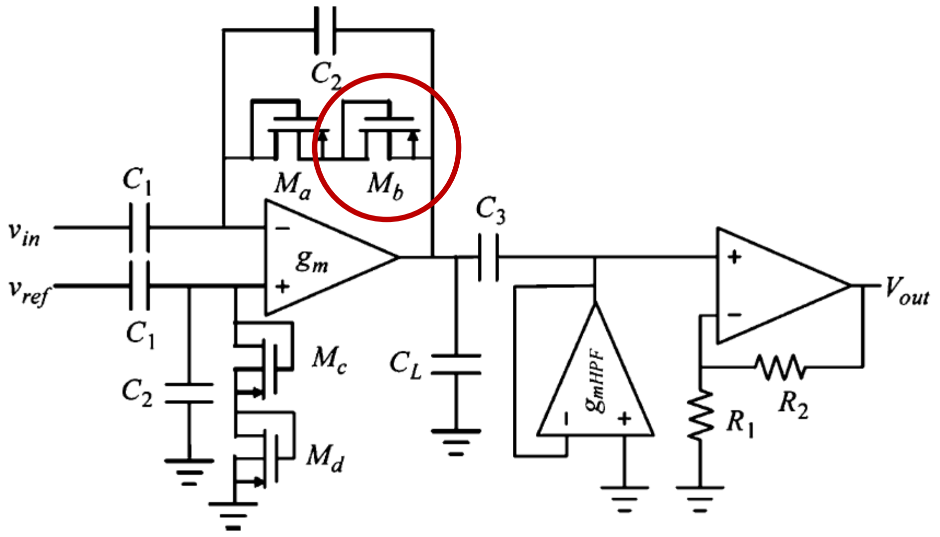
Example of an AP acquisition system

- Single channel amplifier schematic



Example of an AP acquisition system

- Pseudo resistors (diode-connected PMOS in off bias):



+ Very large $R_{eq} \approx 100G\Omega$

+ Very compact

- Very nonlinear

- Extreme PVT dependance

- Light dependent

- Leakage dependent

Example of an AP acquisition system

- Measurement results:

Integrated Neural Interface IC Measured Performance	
Power/command signal frequency	2.64 MHz
Minimum required receive coil voltage amplitude	5.7 V (peak)
3.3-V voltage regulator dropout (I_L = 3 mA)	250 mV
Load regulation (I_L = 2-10 mA)	0.15 %
Line regulation (V_{unreg} = 3.5 V – 8.0 V)	<0.30 %/V
Maximum command input data rate (ASK)	6.5 kbps
Number of Channels/Electrodes	88 signal, 12 ground
Neural Signal Amplifier Gain	60.1 dB (1.1 – 5 kHz)
Input Referred Noise	5.1 μVrms
Individual Amplifier Supply Current	12.8 μA
ADC resolution (LSB = 2.4 μV electrode referred)	9 bits
ADC sampling rate	15.0 kSamples/s
ADC INL/DNL error (codes 50-511)	±0.8 LSB/ ±0.6 LSB
Spike detector threshold resolution (LSB = 4.8 μV electrode referred)	7 bits
FSK data transmission frequency	433 MHz
FSK data rate	330 kbps
Received signal power at distance of 13 cm	-86 dBm
Total chip power dissipation	13.5 mW
Total chip area (0.5-μm, 2P3M CMOS)	27.3 mm^2

High spatial resolution AP acquisition system

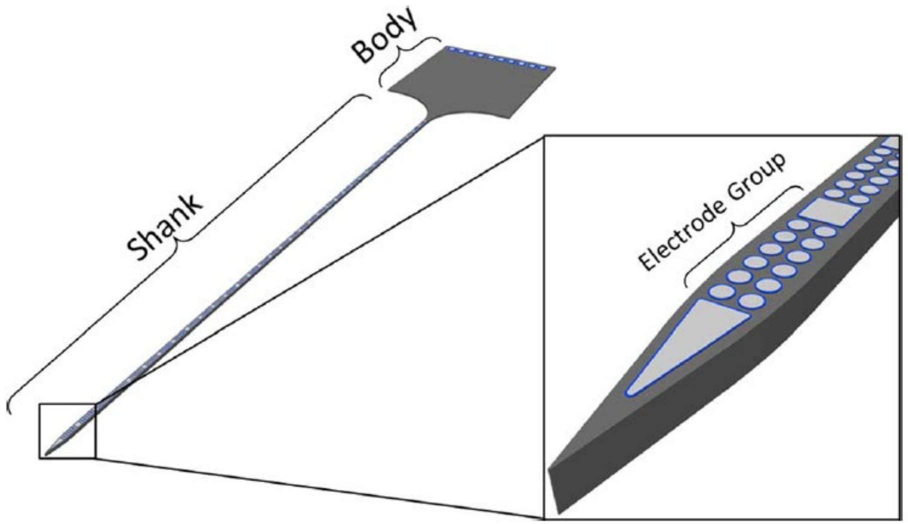
248 IEEE JOURNAL OF SOLID-STATE CIRCUITS, VOL. 49, NO. 1, JANUARY 2014

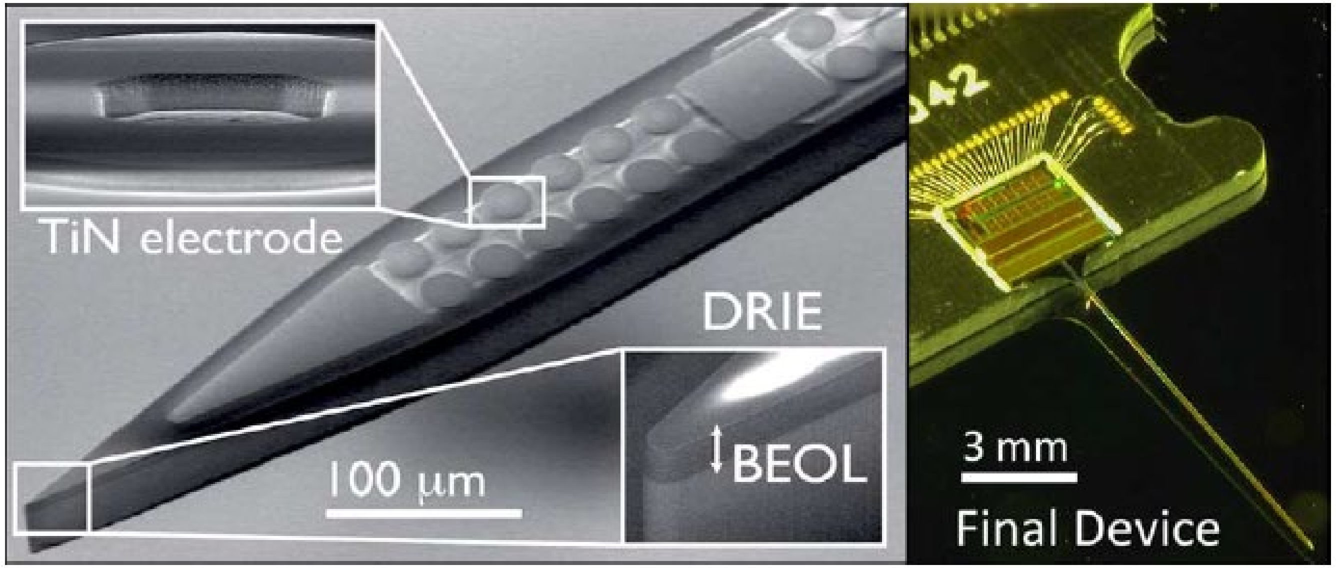
An Implantable 455-Active-Electrode 52-Channel CMOS Neural Probe

Carolina Mora Lopez, Alexandru Andrei, Srinjoy Mitra, Marleen Welkenhuysen, Wolfgang Eberle, *Senior Member, IEEE*, Carmen Bartic, Robert Puers, *Fellow, IEEE*, Refet Firat Yazicioglu, *Member, IEEE*, and Georges G. E. Gielen, *Fellow, IEEE*

- Shank probe with high count of measurement sites

High spatial resolution AP acquisition system





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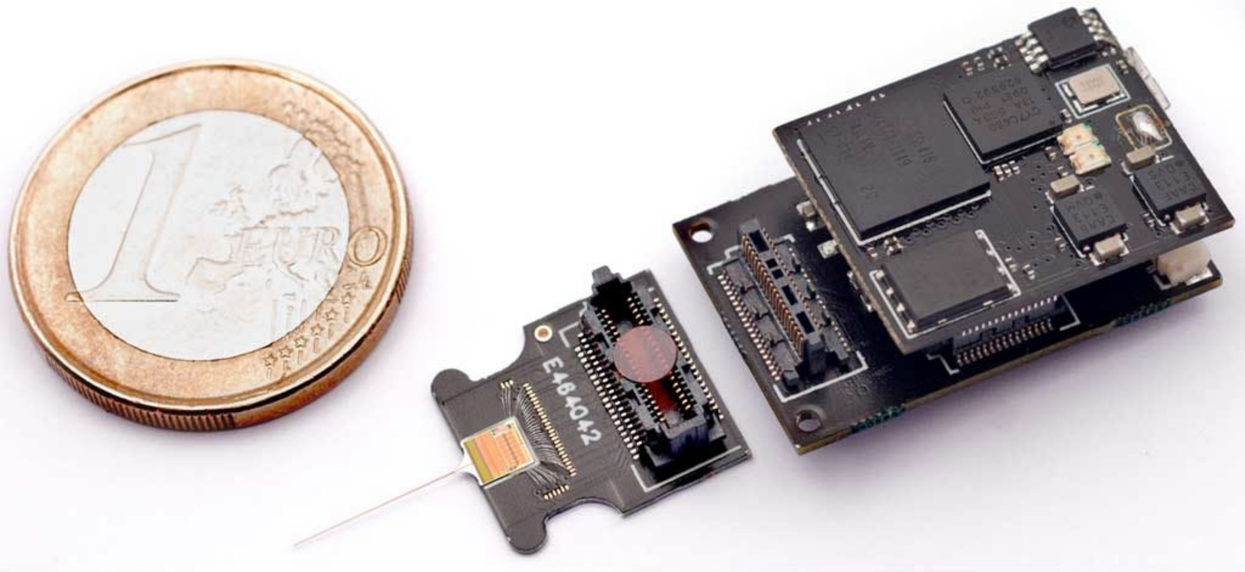
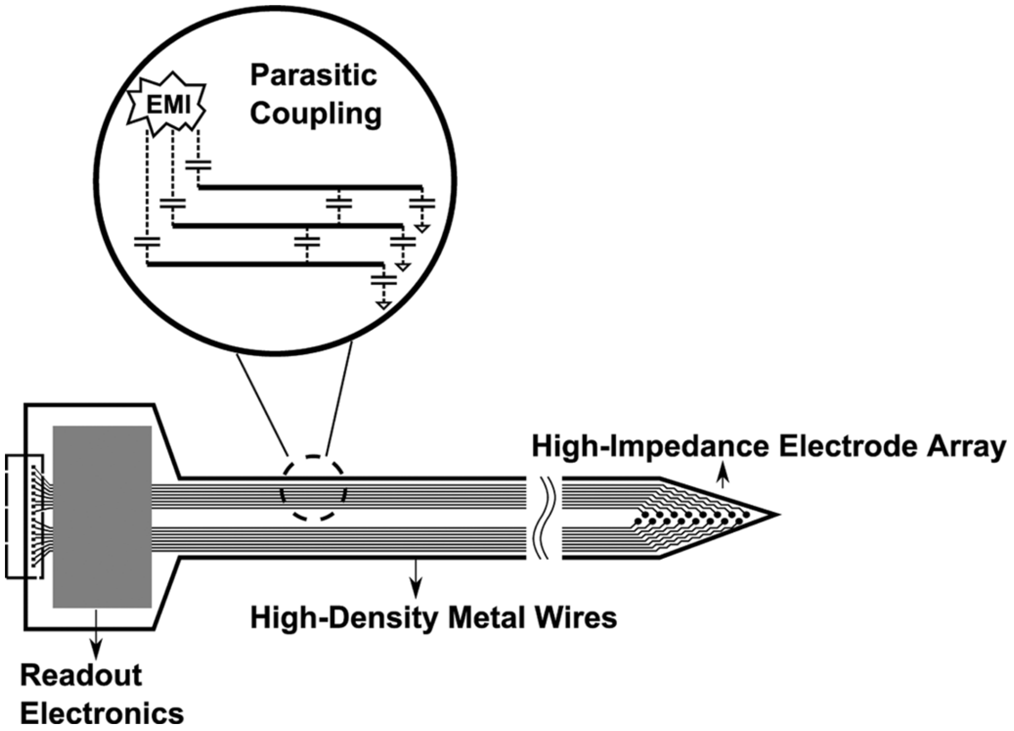
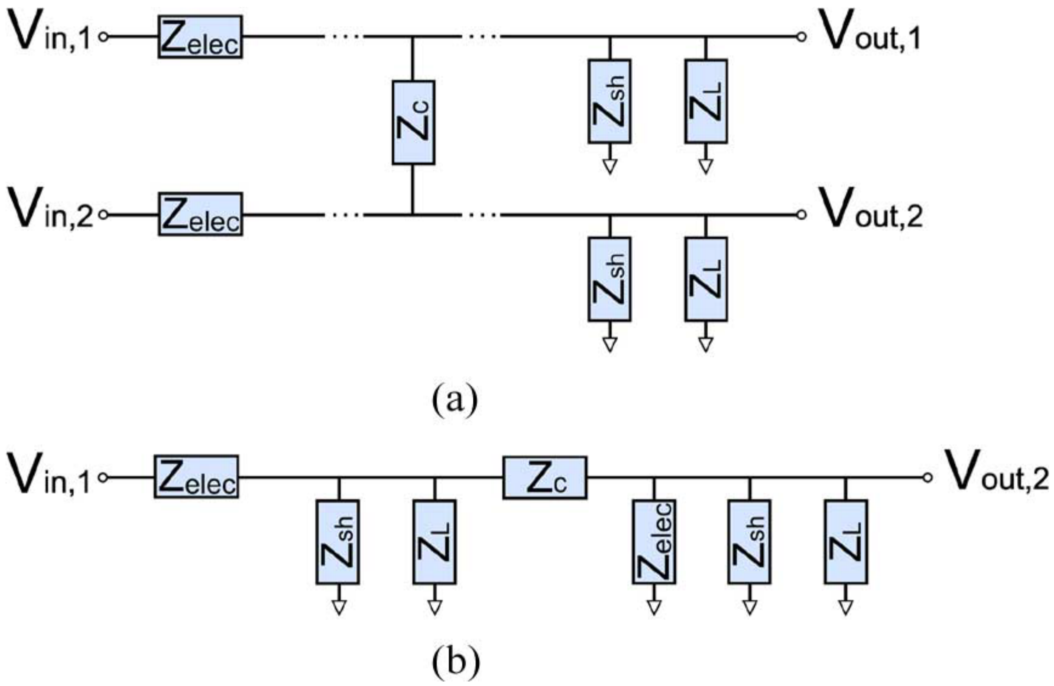
High spatial resolution AP acquisition system



High spatial resolution AP acquisition system

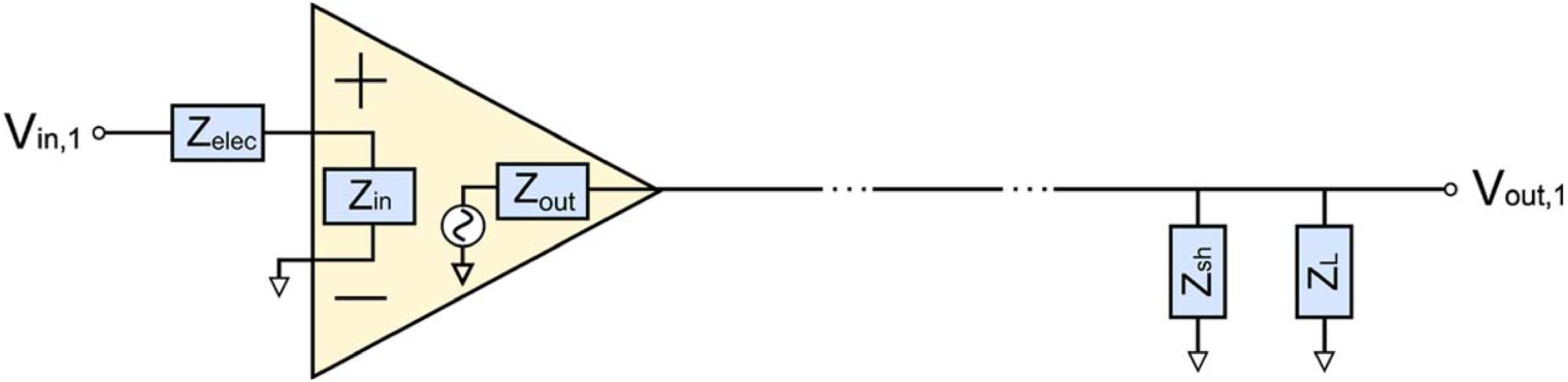
- Interference and cross-talk issues





High spatial resolution AP acquisition system

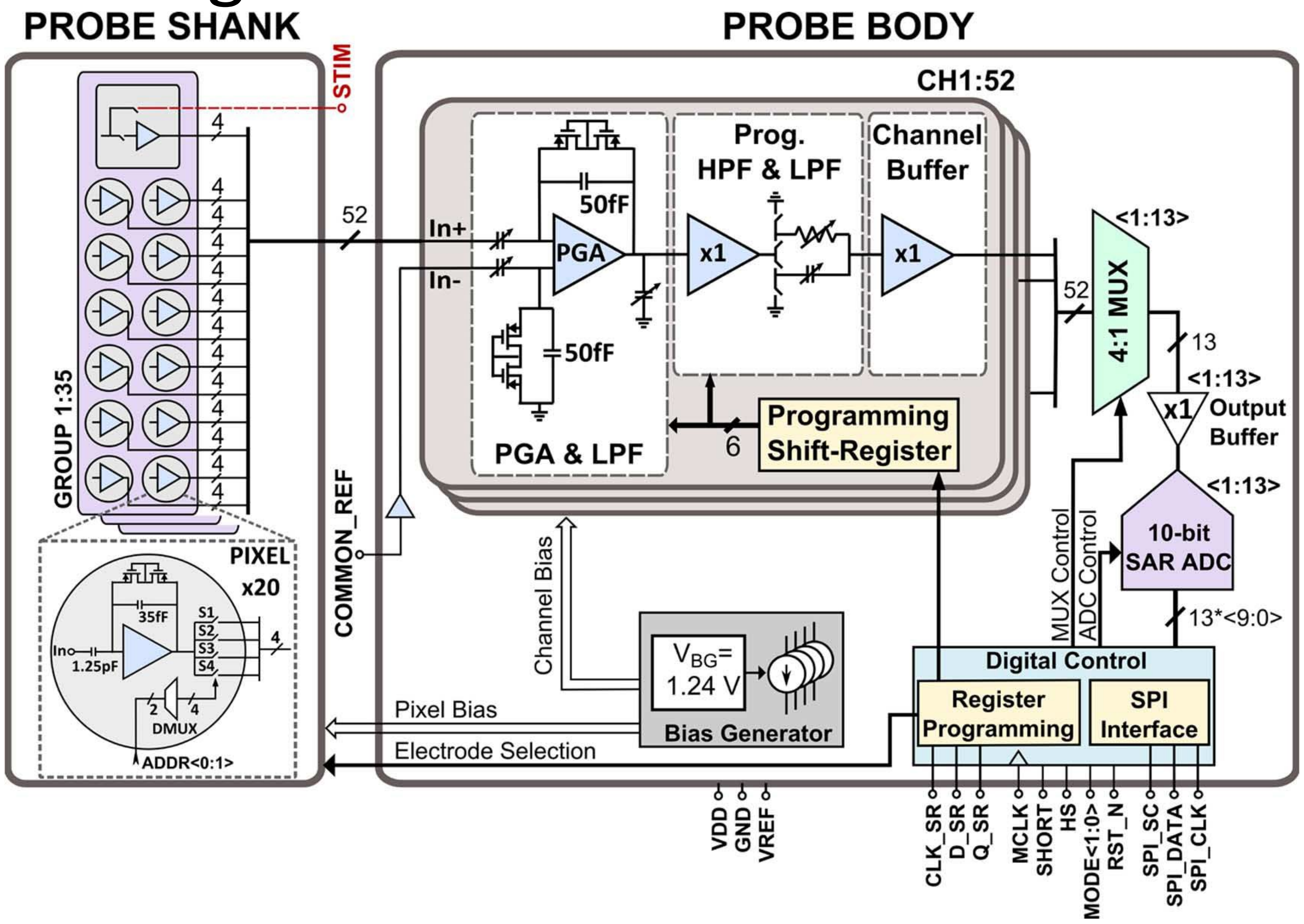
- Interference and cross-talk issues



- Active electrodes

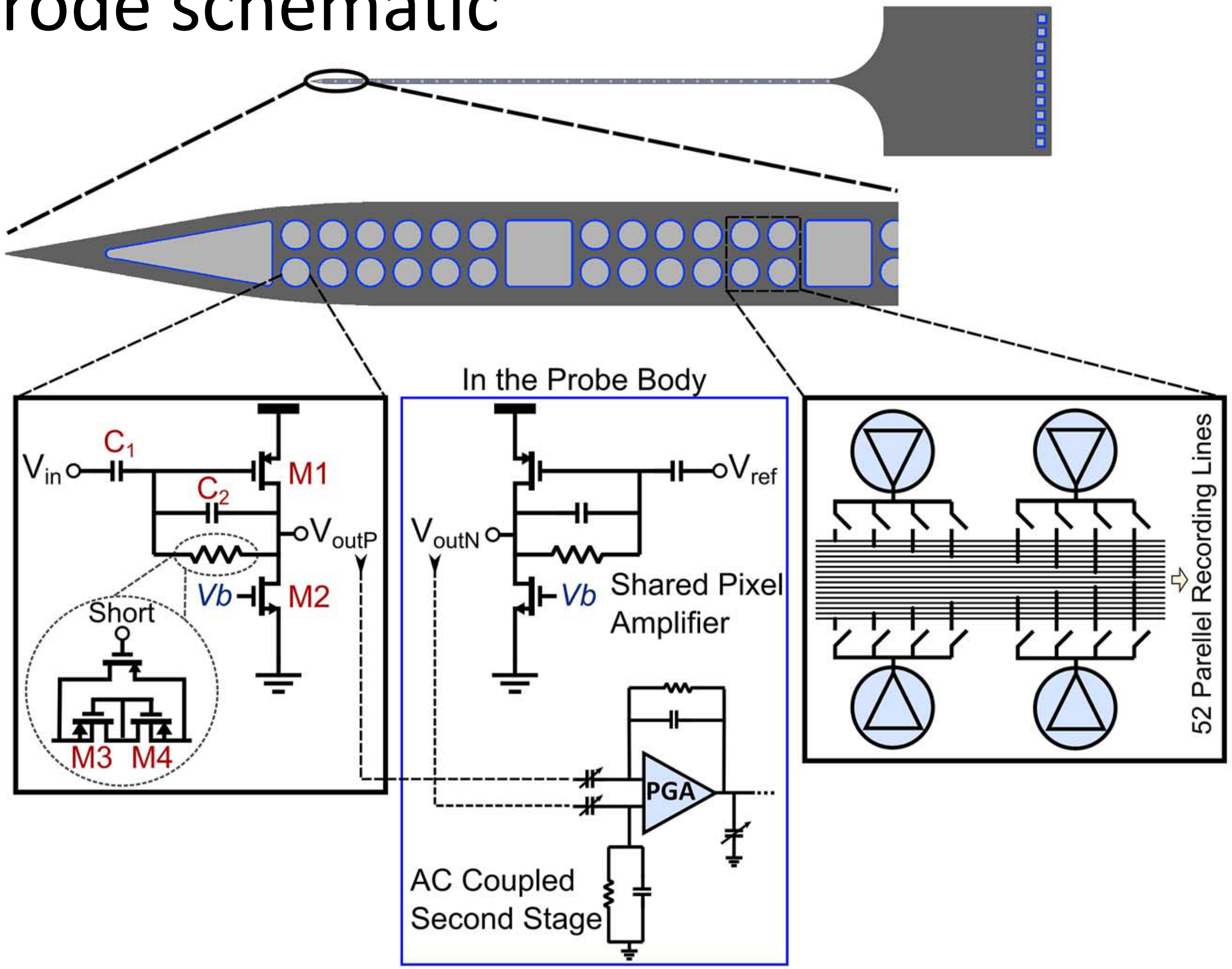
High spatial resolution AP acquisition system

- System block diagram



High spatial resolution AP acquisition system

- Active electrode schematic



High spatial resolution AP acquisition system

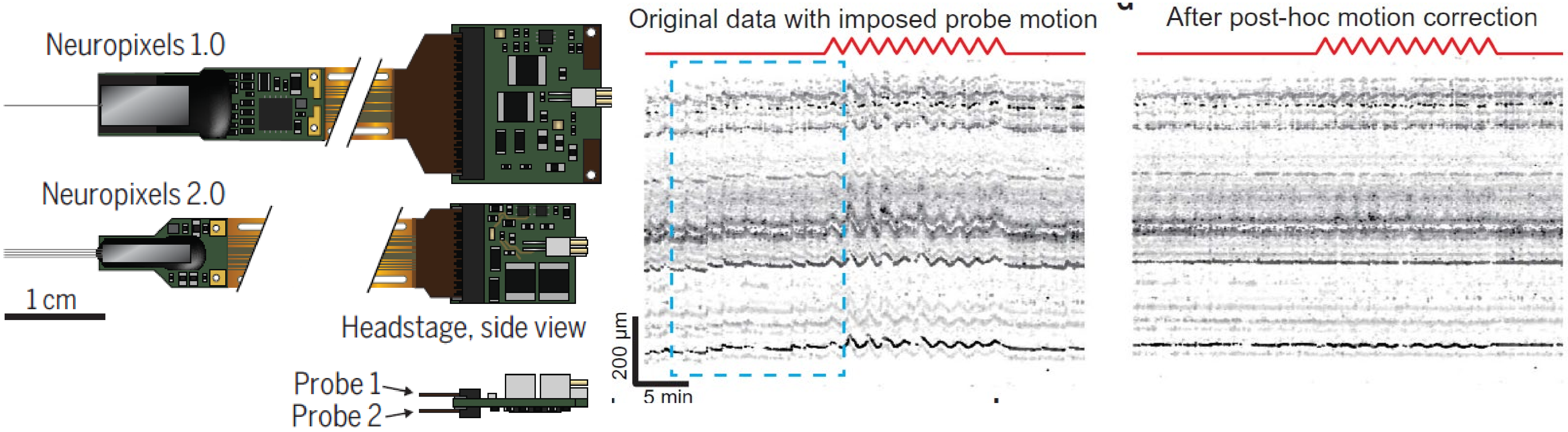
- Measured results

Parameter	*Measured Value*					
	[33]	*[4]*	*[13]*	*[10]*	*[39]*	*This Work*
Probe Shank						
No./Type Electrodes	--	8[A] Passive	64 Passive	257[B] Passive	--	**455 Active**
Electrode Area (μm^2)	--	100	108	1963.5	--	**78.6/491**
Electrode Pitch (μm)	--	100	28	60	--	**35**
Crosstalk (dB)	--	--	-84	--	--	**-44.8**
Readout Electronics						
No./Type Channels	1[D]	8 Integrated	64 Hybrid[C]	128 Hybrid[C]	96[D]	**52 Integrated**
Supply Voltage (V)	0.5	3	3	--	1.2	**1.8**
Total Power/Ch (μW)	5.04	94.5	351.6	39.1	67.7	**27.84**
Total Area/ Ch (mm^2)	0.013	0.625	0.45	--	0.26	**0.19**
Analog Front-End (Pixel Amplifier + Recording Channel)						
Power (μW)	5.04[E]	68	--	--	35	**7.02**
Input Noise (μV_{rms})	4.9	8.9	2	3.7	2.2	**3.2**
NEF	5.99	16	--	--	4.5	**3.08**
PEF= $NEF^2 \cdot V_{DD}$	17.96	771	--	--	24.3	**17.13**
Gain	32	1000	194	70.8	630	**30-4000**
HP Corner (Hz)	300	300	1.3	1	1/280	**0.5/200/300/500**
LP Corner (Hz)	10000	10000	6400	10000	10000	**200/6000**
THD	2%	--	--	--	--	**1% (@ 18mV_{pp})**
CMRR/PSRR (dB)	75/64	--	83/84	--	--	**60/76**
ADC						
Resolution/ENOB (bit)	8/7.2	5/--	--	--	10/9.7	**10/9.2**
DNL (LSB)	0.55	0.33	--	--	0.29/-0.37	**0.23/-0.15**
INL (LSB)	--	0.5	--	--	0.28/-0.33	**0.42/-0.35**
Sam. Rate (kS/s)	20	160 (8 Ch)	--	--	31.25	**120 (4 Ch)**

[A] A 3-D array of 256 sites is achieved by mechanical assembly of 4 multi-shank (8) probes.
[B] In a multi-shank (4) probe with 1028 sites.
[C] Hybrid: Readout circuits are in a separate ASIC.
[D] Neural recording ASIC, not integrated with a neural probe.
[E] Includes ADC.

High spatial resolution AP acquisition system

- Pros: possible to follow brain functioning with neuron resolution
- Cons: difficult to do this for a long time in chronic implants



Source: Steinmetz et al., Science 372, 258 (2021)

Exercise 2

- Answer the following questions:
  a) Why is it possible in the paper by Harrison to avoid chopping and in the one by Denison not?
  b) In the paper by Harrison, why is it a very good idea to add after the amplifier a Gm-C high pass filter?
  c) In the same paper, why the same impedance used in the feedback branch is added between ground and the positive input of the amplifier?
  d) Which amplifier is more efficient, the one by Denison or the one by Harrison?
  e) Why does the paper by Mora Lopez use a PMOS common source in the active electrode amplifier?

Exercise 2: answers

a) As the paper by Harrison deals with Action Potentials, which are signals at relatively high frequency (>100Hz), he can filter out the low frequency spectrum and get rid of the 1/f noise in this way. The paper by Denison deals with NFPs, which are at very low frequency (their spectrum extends below 1Hz), and thus Denison cannot use this method to attenuate the effect of 1/f noise.

b) The Gm-C filter indeed implements the high-pass behavior that cancels at the output the 1/f noise added by the electronics.

c) In this way, the impedance seen from the input V_{in} to ground is made as similar as possible (matching) to the one seen from V_{ref} to ground. Then, if a common mode disturbance is applied to V_{in} and V_{ref} , it will appear at the differential amplifier inputs still as common mode and will be rejected by the CMRR. An imbalance between the two branches would results in a different voltage at the amplifiers inputs for the same input disturbances at V_{in} and V_{ref} , and thus parts of the input common node would be converted to a differential signal and would propagate to the output. Please note that the amplifier output is low impedance (and thus almost at ground for the signal) due to the feedback applied.

d) Calculate the NEF for both amplifiers to answer this question. The BW by Harrison is 1.1kHz-5kHz.

e) Because it needs to implement an amplifier that is very compact, due to the space restrictions in the neural probe.

Summary

- Capacitive feedback amplifiers for neural interfaces
- Design trade-offs
- Advantages and problems caused by chopping
- Active vs. passive electrodes